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Public Health

The order in this section is:—**General; Vital Statistics; Epidemiology; Maternal and Child Health; Health of Students, Nurses and Hospital Staffs; Health of Old Persons and the Chronically Ill; Chronic Cardio-Respiratory Diseases; Chronic Rheumatism; Cancer; Miscellaneous Diseases; Dental Health; Mental Health.**

GENERAL

NORWEGIAN FOUNDATION FOR ASSISTANCE TO UNDERDEVELOPED COUNTRIES. **The Indo-Norwegian Project in Kerala. Report No. 5. Health Survey from the Project Area for 1957** [BARSTAD, L. & SAETRE, Gerd (Prepared by)], 94 pp. illustrated. 1960. Oslo: Indiafondet, Klingenberggaten 7, Norway.

The first 4 reports of the Indo-Norwegian Project in Kerala were reviewed in this *Bulletin* [1960, v. 35, 97]. This report continues the description of medical and sociological work done. It is difficult to pick out salient points in such a record of work, and in the main the reviewer must be content with calling attention to the amount of information on a rather primitive rural area that is accumulating in these reports. Anyone searching for detail on any related subject will do well to look in them. Although the importance of preventive medicine has been constantly emphasized, this aspect has always been hampered by the urgent demand for curative services. A curative clinic, giving free treatment to all inhabitants of the area, was set up in 1957. The existence of medical facilities has caused some population movement into the area, for the population grew from 11,160 in 1953 to 15,296 by the end of 1957. Even a high excess of births over deaths (the figure for 1957 was 531) cannot account for such an increase.

Information is given of age distribution, occupation, housing, water, sanitation, average debts. On the clinical side, morbidity details still depend on attendances at the clinics. *B. B. Waddy*

VITAL STATISTICS

UTTLEY, K. H. **The Birth, Still-Birth, Death and Fertility Rates in the Coloured Population of Antigua, West Indies, from 1857 to 1956.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1961, Jan., v. 55, No. 1, 69–78.

In contrast to the birth rate in England and Wales, which has fallen steadily during the past 80 years and is now less than one-half of its former level, the birth rate in Antigua has fluctuated around a fairly constant level and in 1947–56 it was 32·8 per 1,000 living, being the same as the rate in England and Wales in 1881–90. The birth rate per 1,000 females aged 15–44 years in Antigua varied between 140 and 145 during the past 80 years. The rate in England and Wales, which was slightly below the rate in Antigua in the beginning of the period, steadily declined to one-half of its initial level. In 1947–56 the rate in England and Wales was 76 compared with 144 in Antigua. Although stillbirths were not registered in England and Wales until 1928 they have been registered in Antigua since births and deaths were first registered in 1856. The stillbirth rate has fallen steadily in Antigua since 1867–76 when it was 125 per 1,000 total births to 32 in 1947–56. The stillbirth rate in England and Wales in 1947–56 was 24.

The crude death rate in Antigua has fallen from 37·2 per 1,000 in 1867–76 to 9·4 in 1957–58 and the standardized death rate shows a fall of the same magnitude. For the various census years the death rates have been given by age and sex. The male death rate was greater than the female at all ages and, with a few exceptions, in every age group. The female death rate has fallen faster than the male. The fall in the death rate has been greatest in childhood where the rates are about one-fifth of the former level. Between ages 15 and 65 the female death rate is one-third and male rate slightly less than one-half of the initial level. *W. J. Martin*

EPIDEMIOLOGY

COHEN, J., YOFE, J. & DAVIES, A. M. **Family Morbidity. A Suggested Method of Measurement.** *Brit. J. Preventive & Social Med.* 1960, Jan., v. 14, No. 1, 39–43, 4 figs.

These authors have worked out a statistical method for the study of family morbidity which, they claim, can be used to identify suitable groups for special study or for medical care.

450 families were housed in an estate provided for new immigrants in Kiryat Yovel, a Jerusalem suburb. A list of 150 of these families (a 1 in 3 sample) was prepared. From this list a sub-sample of 30 families was initially chosen for detailed investigation, but was found to be so heterogeneous in racial origin that it was decided to concentrate on 20 of these families who came from Near Eastern or North African countries. 26 other families with typical North African names were picked from the list of 150, making a total study population of 46 families.

"Family sheets" were prepared for each year, in which the number and type of episodes of disease were tabulated according to month and family member. For the first 26 families the sheets were compiled for the 3 years 1955–57 from the family files of the physicians of the Haddasseh Community Health Centre. The sheets for the next 26 families were compiled, for 1956 and 1957 only, from the individual consultation sheets of the physicians. The data from the 2 sources gave very similar results and could therefore be pooled.

The number of "contacts" (*i.e.*, physician consultations) for all conditions and for acute respiratory and for acute gastro-intestinal illness were computed. The numbers of contacts were then grouped according to the age and sex of each individual, and total age-sex-specific consultation rates per year were calculated for all the 46 families. By applying these rates to the individual members of each family in each year and adding the results, an expected number of consultations was obtained for that member over the period of observation. Summation of the individual expected numbers gave an expected number for the family. Division of the observed by the expected number then gave "consultation-indices" for each individual and each family.

The distribution of these indices for all conditions showed a tendency for the members of a family to resemble each other, *i.e.*, the differences between families were more marked than those within families. The family indices for all conditions showed a significantly high correlation between 2 different years. Significantly high correlations were also found between the family indices for respiratory illness and those for gastro-intestinal illness, and between these and the corresponding indices for all other illnesses. This suggested that there were consultation-prone families, irrespective of any susceptibility to special types of disease.

A. S. Fairbairn

UNITED STATES DEPT. HEALTH, EDUCATION & WELFARE. **Health Statistics from the U.S. National Health Survey. A Study of Special Purpose Medical-History Techniques. A Methodological Study of Special Purpose Medical-History-taking Procedure applicable to Population Surveys based on Health Examinations.** *Pub. Health Service Publication No. 584–D1.* pp. ii+27. 1960, Jan. Wash., D.C.

A methodological study of the use of a medical history questionnaire in a health survey is described. From the outset, it was found that people were prepared to discuss their medical histories quite freely, anyway for the purposes of this research. With regard to the design of the form, after preliminary trials it was decided to put questions relating to symptoms before those relating to disease, and the more common symptoms before the less common. After trying 3-point and even 5-point measurement scales for frequency and intensity of symptoms, a 2-point scale was found to be preferable as it was more meaningful to the people being interviewed.

Three methods of obtaining the information were compared:

(1) The use by an interviewer of a questionnaire containing "open" questions—that is, general questions which require the respondent to frame his own answers.

(2) The use by an interviewer of a questionnaire containing "closed" questions—that is, questions so framed they can be answered simply with a "yes" or "no", or along some dimension specified in the question.

(3) The use of a questionnaire containing "closed" questions, but completed by the respondent, without the help or guidance of an interviewer.

The open questionnaire obtained considerably fewer reports of symptoms and illnesses than did the closed questionnaire, whether this was self-administered or completed by an interviewer. Furthermore, the answers to the closed questions give better quantitative measures for comparison and analysis. However, the open questionnaire gave better information on the background of the respondent's problems. It is concluded that the main instrument for this type of survey work should be a predominantly closed-question questionnaire, although it may contain a few open questions. There was no marked evidence that the interviewer-administered form showed any superiority over the self-administered form in obtaining reports on the number of symptoms and illnesses with the single exception that the interviewer-administered form revealed a history of childhood illness more frequently.

The interviews were conducted by trained non-medical interviewers, or by nurses who had been given some training in interviewing techniques. The nurses wore their professional uniforms for some of the interviews conducted by them. There was a slight indication that the lay interviewers obtained higher frequencies of symptoms than the nurses, whether in uniform or not, and that the lowest frequencies were obtained by the

nurses in uniform. The numbers were not large enough to exclude the possibility that the observed differences were a result of chance. It was also found that persons who were not medically trained could be trained as interviewers in a shorter time than could nurses, but the lay interviewers had more difficulty in spelling the names of drugs, operations, and illnesses and were less able to help when the respondent misremembered technical terms.

The respondents were interviewed or given the self-administered questionnaire on two occasions at an interval of 1–2 weeks. Comparisons between the answers on each occasion showed a relatively high degree of reliability or consistency of reply. Accuracy was not evaluated. Reports on illnesses were quite reliable, but there was some variability for symptoms. Serious symptoms and symptoms with physical signs were reported with a higher degree of reliability than others. Throughout this study the criterion for success was the number of symptoms or of illnesses which the person reported, the underlying assumption being that it is better to obtain false positives than false negatives.

The project reported here is only one part of a wider study being conducted into methods for the collection of the different types of health data. Its limitations were, in fact, the boundaries laid down at the outset. This is a valuable study, lucidly discussed and presented.

M. D. Warren

STEIN, Lilli. **Morbidity in a London General Practice. Social and Demographic Data.** *Brit. J. Preventive & Social Med.* 1960, Jan., v. 14, No. 1, 9–15, 2 figs.

Dr. Stein's study is one of a series undertaken by the staff of the Institute of Psychiatry into the incidence of psychiatric disorder in the general population outside hospital. She first describes in detail the social and demographic features of a population which provides the basis for other studies in the series. This was a 20% sample of a practice of 9,000 patients run by 2 men and 2 women general practitioners in a working-class residential area in outer south-east London. Only those patients who were in the practice for a whole year (March 1956–February 1957) were included. Certain measures of frequency of consultation are then related to the characteristics of this population.

The stability of the practice was shown by the fact that half the study population had been patients of the practice since before 1949. A slight excess of children under 15 and of adults aged 30–40 compared with south-east London as a whole was accounted for by the special facilities offered in this practice to parents for their small children.

Family and social data were collected on a sample of households called the "questionnaire section", comprising about 50% of the practice patients. Half of this group were chosen randomly for questioning, and the other half by questioning those patients who attended the surgery in the summer following the study year, about their households. This latter group were not therefore truly representative of the whole practice and contained a higher proportion of parents with their young children. Thus there were 2·1 patients per address in the whole study population, but in the questionnaire section there were 3·49 persons per household and 2·73 persons per patient-group (*i.e.*, the household, excluding those members of it who were not patients of the practice). Non-patient members of these households were usually men; women and children had a tendency to attend the same doctor.

The questionnaire households were larger than those in England and Wales as a whole and contained more children under 16. 42% of these families had lived in the same house for 10 or more years. There was a very small excess of persons in Social Class III and a corresponding deficit in Social Class IV and V compared with England and Wales, but this discrepancy was confined to larger households: smaller households were no different in social class distribution from the country as a whole. About 20% of wage-earners had been in their present job for over 15 years, and 9% had changed their job in the last year.

In 92 households chosen randomly, a medical history was obtained from each member or from a relative. One-third of families gave a history of psychiatric illness, almost always among first degree relatives. This history was mostly of admission to a mental hospital, but in a few cases there was a mental deficiency or illness treated at home. In less than half the families there was no such history, and in some of these the practice records suggested that it had been suppressed.

The frequency of attendance in the whole study population was 3·9 consultations per patient per year (in the middle of the range found in other general-practice studies). Among those patients who attended the surgery during the year the average number of attendances was 5·6. Under the age of 15, boys attended more often than girls, but over 15, women attended more often than men. The mean number of illnesses per attender was 2·4, each illness causing on the average 2·5 consultations. More than one-third of the adult attenders had only one illness. The number of consultations both per illness and per attender increased with age in each sex, but the mean number of illnesses and the percentage of attenders in the whole study population showed no such increase, except for a small rise in the percentage of attenders in older men. Frequency of attendance showed no clear association with social class. It decreased with job duration. Married women in part-time employment showed a slightly lower percentage of attenders, but more complaints per attender than those in full-time jobs.

The percentage of attenders decreased with the length of time during which patients had been registered with the practice. In a study of patients who had been at risk for both the study year and the previous year, 20% had not attended for 2 years. 17% of patients, at risk for 3 years, were 3-year non-attenders. These figures, however, may have been inflated by patients who had left the practice but whose cards had not been removed.

As would be expected, there were differences between the patients attending the men and the women doctors. 56% of the men doctors' patients, but only 24% of the women doctors' patients, were men. Men patients of the women doctors were very frequent attenders.

A. S. Fairbairn

ENTERLINE, P. E. & STEWART, W. H. **Estimated Morbidity in the United States based on Monthly Labor Force Report.** *Pub. Health Rep.* Wash. 1960, Dec., v. 75, No. 12, 1151–60, 5 figs. [11 refs.]

Monthly interviews of representative samples of the civilian population of the United States of America have been carried out by the U.S. Bureau of Census since 1943 in order to estimate the size of the total labour force and other related facts. Since 1947 monthly estimates have been published of the number of persons aged 14 years and over who, because of illness, did not work in the week preceding interview. From 1947 to 1956 about 21,000 households were interviewed each month, and after April 1956 this number was increased to 35,000. The data relating to illness were obtained from answers to a set of questions, which are given and discussed in a technical note, asked by many interviewers. The purpose of the analysis now reported was to judge the usefulness of the "Monthly Labour Force" sickness estimates by comparing them with those of sickness data obtained from the Armed Services and the "National Health Survey". Most of these comparisons were made in terms of seasonal and non-seasonal time trends.

2 diagrams and a table show the "prevalence of illness" rates for each month from July 1947 to September 1959 for the employed civilian labour force obtained from the results of the interviews, and for the Army, Navy and Air Force from reports of persons not available for duty because of medical reasons. The data of the Air Force and Navy are available only from 1949. The percentage of the interviewed civilians who were absent from work for one week or more is used as the prevalence rate for the civilian estimates, while the percentages of available man-days lost through illness is the prevalence rate used for the Armed Forces' estimates. [It should be noted that the Air Force and Navy data include those relating to the overseas forces while the Army data do not, and that the Navy and Army data exclude battle injuries while the Air Force data do not.]

The monthly prevalence rate for the civilians followed no obvious trend over the 12 years and varied between 1 and 2%. The rates for the Armed Forces in some years were clearly associated with periods of active service, but generally between 1955 and 1959 all 4 series have surprisingly similar rates. It is suggested that while higher rates might be expected in the Armed Forces because of the inclusion of short illnesses (*i.e.*, of less than one week), this might be balanced by increased rates due to the older population in the civilian data. Possibly of more interest is the apparent agreement of the seasonal trends in the 4 series with peak rates in February and low rates in the summer months. This trend has also been observed in other civilian sickness surveys in the U.S.A.

Since May 1955 some additional data have been obtained at the interviews about reasons for part-time work in the week preceding interview. This information has been used, in combination with that already discussed, to derive prevalence rates for all illness irrespective of duration and these rates are expressed as the percentage of the employed civilian labour force absent on an average work day because of illness. Diagrams show these rates for each quarter from the 3rd quarter of 1955 to the 3rd quarter of 1959. Since 1957 prevalence rates are also available from the "National Health Survey" in which information about illness in the "usual working" population is also obtained by interviewing a representative sample of the population aged 17 and over. In the National Survey prevalence rates are estimated as the percentage of available man-work days lost through illness and the quarterly rates followed the same seasonal pattern as those obtained from the "Monthly Labour Force" interviews. Apart from the first few quarters (late 1957 and early 1958) the levels of the rates were also very similar.

So-called "excess monthly prevalence rates" [*i.e.*, residual rates after the removal of expected seasonal and secular trends] are represented diagrammatically for each month from July 1947 to September 1959 from the "Monthly Labour Force" statistics. In these the influence of the 4 influenza epidemics of March, 1950, March, 1951, February, 1953 and October/November, 1957 are clearly indicated by peaks in the residuals.

The authors conclude that "Generally, information on illnesses reported in 'The Monthly Report on the Labour Force' would seem to be a valuable supplement to other data regarding illness patterns and trends in the United States". *E. A. Cheeseman*

LUE, Hung-Chi. **Statistical Study on the Leading Causes of Death among Inpatients of the Pediatric Department of National Taiwan University Hospital.** *Mem. College Med. Nat. Taiwan Univ.* 1960, Mar., v. 6, Nos. 1/2, 57–69, 6 figs.

This analysis is based on the deaths of 1,145 children aged under 15 years of age in the National Taiwan University Hospital during the 12 years 1946–57. Pneumonia and diarrhoea, enteritis etc. are important causes of death throughout childhood. Tuberculosis and summer encephalitis become important after the first year of life. The death rate from neonatal tetanus was very large among infants in this study and was second as a cause of neonatal mortality to pneumonia and was slightly larger than the death rate from prematurity.

Comparisons have been made with other studies in Taiwan (Maternal and Child Health Project, etc). There are some differences in the methods of classification of the causes of death, *e.g.* 32% of the neonatal deaths in the Maternal and Child Health Project were due to congenital debility but in the Hospital study no deaths were attributed to this cause. Measles does not appear as a cause of death in the Hospital study, the deaths being attributed to the fatal complication but in the Maternal and Child Health Project the deaths were shown as due to measles. Despite these differences there is agreement between the various investigators that the leading causes of infant mortality are pneumonia, etc; diarrhoea, enteritis, etc; and tetanus.

W. J. Martin

RODENWALDT, Ernst & JUSATZ, Helmut J. [Edited by.] **Welt-Seuchen-Atlas.** [World Atlas of Epidemic Diseases] Part III. 3rd issue. pp. III/67–III/70, III/75–III/78, III/83–III/86, III/107–III/110, III/123–III/136, 1 text fig. & 10 folding pp. of coloured maps. [Numerous refs.] 1959 [In German & English.] Hamburg 1: Falk-Verlag, Burchardstrasse 8. [Dm. 63.]

[A review of this book appears in the *Tropical Diseases Bulletin*, 1961, v. 58, 649.]

CHRONIC CARDIO-RESPIRATORY DISEASES

OGILVIE, A. G. **Social and Environmental Factors in Chronic Bronchitis in Newcastle upon Tyne.** *Postgraduate Med. J.* 1960, Apr., v. 36, No. 414, 261–9, 7 figs. [25 refs.]

Dr. Ogilvie's paper is one of a series of contributions to a symposium on medical activities in the Department of Medicine at Newcastle upon Tyne. Much of the material presented here has been reported on elsewhere and is derived from an extensive survey of chronic bronchitis carried out by the author and his colleagues in Newcastle in 1955–56. The well known contrasts between urban and rural mortality and the probable role of atmospheric pollution are exemplified in Newcastle by the higher proportion of persons with bronchitis (67%) who lived in the enclosed type of locality in which the houses are crowded together with little intervening space, compared with the proportion of healthy individuals (54%). Both Newcastle and Gateshead, which lies opposite Newcastle across the river Tyne, are polluted towns, and the degree of atmospheric pollution is greatest near the river, falling off with distance from the river and increasing height above sea level. In Newcastle the land flattens out at about 300 ft., and beyond this, in the most northern area of the town, the new open type of housing is predominantly found, but even in this type of locality the enclosed type of housing which remains is still associated with an increased prevalence of bronchitis. These findings suggest that the effect of enclosed housing aggravates the effect of any existing atmospheric pollution. *A. S. Fairbairn*

CANCER

CARTWRIGHT, Ann, MARTIN, F. M. & THOMSON, J. G. **Health Hazards of Cigarette Smoking. Current Popular Beliefs.** *Brit. J. Preventive & Social Med.* 1960, Oct., v. 14, No. 4, 160–66, 2 figs.

Different samples of the population of Edinburgh were interviewed in May and November 1958, before and after a local health education campaign. Samples of 780 and 782 adults were drawn from the electoral register and 76% were successfully interviewed on each occasion.

It was generally agreed that smoking (certainly heavy smoking) was potentially harmful to health and most thought that it might cause or aggravate cough, breathlessness, bronchitis and catarrh. More than half thought it might aggravate tuberculosis and gastric ulcer. Nearly all (98%) had heard that smoking might cause lung cancer; 19% accepted this theory without qualification and 33% partially accepted it. Acceptance of the theory was related independently to the individual's smoking habits and to his social class; non-smokers and persons in the higher social classes accepted the theory more readily than smokers and unskilled workers. Many believed that the danger of lung cancer arose only above a certain level of consumption; the level varied with the amount smoked and tended to be a little above that normally smoked by the individual.

Substantial majorities of both smokers and non-smokers favoured the banning of smoking in cinemas and theatres and about half (more particularly non-smokers) approved of similar restrictions in buses and restaurants. *Richard Doll*

RELE, J. R. **Demographic Approach to the Problem of the Connexion between Lung Cancer and Smoking.** *Brit. J. Preventive & Social Med.* 1960, Oct., v. 14, No. 4, 181–4.

Death entries for the years 1957–58 were examined in the records of the Bombay Municipal Health Department. Data relating to the sex, age and religious faith of the subject were extracted for all persons dying of cancer. Comparison of the cancer mortality among Parsees and persons of other religious faiths showed that the crude annual mortality per 100,000 was much higher among the Parsees (90 for men and 109 for women) than among the others (23 for men and 20 for women). This difference was, however, largely due to the longer expectation of life of the Parsees. Rates standardized for age were calculated from estimates of the age distribution of the two groups and these showed little difference between the male rates (90 per 100,000 for Parsees, 81 per 100,000 for others), but the female rate was still substantially higher among the Parsees (109 against 53 per 100,000).

The standardized death rate from lung cancer was

about 5 times higher among non-Parsee males than among non-Parsee females. Among Parsees the rates were equal in both sexes. The number observed among Parsee males was significantly less than the number expected at non-Parsee rates (2 against 7·5); the number observed among Parsee women was close to the expected number (2 against 1·5).

Smoking is extremely rare among all groups of Indian women; it is also uncommon among Parsee men—since it is forbidden by their religion. Smoking is, however, common among other groups and these observations support a causal relationship between smoking and lung cancer. *Richard Doll*

See also p. 445, NAU, NEAL & STEMBRIDGE. **A Study of the Physiological Effects of Carbon Black. III. Adsorption and Elution Potentials; Subcutaneous Injections.**

MISCELLANEOUS DISEASES

DE SMET, M. & DE VISSCHER, M. Contribution à l'étude de l'endémie goitreuse des Uélés (République du Congo). [**Endemic Goitre in the Uélé District of the Congo**] *Ann. Soc. Belge de Méd. Trop.* 1960, Aug. 31, v. 40, No. 4, 601–22, 2 maps & 2 figs. [Numerous refs.]

The inhabitants of the Uélé River (or Welle River) District on the north side of the River Congo (former Belgian Congo) have an incidence of endemic goitre which is probably among the largest in the world. Reports on this endemic goitre area have been published in the last few years by the senior author of the present paper. In this there is an account of a study of iodine insufficiency in that area in the Congo.

The area studied has a population of about 500,000 and 3 zones of endemicity are recognized—small incidence 5–20% of goitre, medium 20–50% and a hyperendemic zone where between 50% and over 90% of adults and children are affected. A map of the area is given.

There is an account of the pathological anatomy of 173 goitres removed by operation which were examined histologically. A high proportion of goitres were found to be of nodular type.

Tables set out the amounts of iodine found by chemical examinations in the waters of the endemic region. In these rivers the iodine content ranged from 0.10 to 0.62 μgm. per litre as compared with 2.37 in the river Congo (at Isangi).

There is discussion of the part played by iodine lack in the causation of goitre with mention of the other possible factors of calcium and magnesium hardness of water and goitrogens in the food.

In a section of the paper the clinical observations are recorded. Severe dysthyroidism was found to be rare except in the hyperendemic area where cretinism of all degrees of severity exists.

Some work on protein-bound iodine in the blood showed the great frequency of insufficiency of thyroid secretion in goitrous patients. *M. E. Delafield*

MENTAL HEALTH

EAST AFRICAN MED. J. 1960, June, v. 37, No. 6, 443–85. [21 refs.] **World Mental Health Year, 1960.**

The whole of this issue of the *East African Medical Journal* is devoted to mental health, and comprises 7 papers contributed by different authors, some of whom have had extensive experience in investigating mental disturbances in Africans. There is no indication that they were papers read at a meeting or conference.

J. R. REES (*Problems of Mental Health in our Time*, pp. 443–447) looks at the problems broadly, noting the advances that have been made in approach and understanding, and the increase which is apparent in neurotic illness and which seems to be related to social change.

E. L. MARGETTS (*The Future for Psychiatry in East Africa*, pp. 448–456) comments on the clinical, research, promotion and teaching aspects of this subject, and here the factors of provision and organization of the relevant services are in the early stages. But apart from the provision of hospitals and staff to administer the appropriate treatment, the author stresses the importance of knowing and understanding the social and cultural background of the African and other inhabitants, stressing the value of social research.

C. [J.C.D.] CAROTHERS (*Further Thoughts on the African Mind*, pp. 457–463) refers to his original epoch-making publication *The African Mind in Health and Disease* [see this *Bulletin*, 1954, v. 29, 281]. His later experience has confirmed his earlier view that "the mental attributes of Africans are the direct outcome of their culture," and he quotes from the writings of other investigators, in and out of Africa, to support his view that this is a world-wide phenomenon, and that of the changes which alter the culture as time goes on, literacy is one of the most important. "The old non-literate cultural modes had, from our point of view, the great shortcoming that they held the clock back. But as a corollary, this did ensure that the world a man was born into was culturally the same world that he died in, and the longer he lived the better he understood that world."

The author makes the point that "the African way of life . . . must in general be well-suited to man's needs since it surely persisted for long ages with very little change; and that it is we who are treading the strange and dangerous path".

T. A. LAMBO (*The Concept and Practice of Mental Health in African Cultures*, pp. 464–471) also comments on the importance of anthropology and sociology, but with the proviso that the psychiatrists are interested in the conditions and consequences of interactions between men living in societies, in terms of mental health. "We recognize that no explanation of the psychological structure and function can be complete which fails to take into account the origin and evolution of the society and at the same time to render comprehensible all its striking and essential features." He goes on to discuss the physical and intellectual changes (as in education) which are altering African life deeply and rapidly, and acknowledges that the speed of change—for instance of Western methods of treatment of disease—has been too great for the Africans. He therefore does not underrate the "indigenous psychotherapeutic approach in the total management of the patient" and its effect in reinforcing the patient emotionally.

Tigani EL MAHI (*Concept of Mental Health*, pp. 472–476) approaches the subject historically, and shows how medicine in the past was related to religion, and how the notion of disease, as due to interference of gods or the spirits of the dead, grew up in such circumstances. These ideas were potent, and "The criterion of acceptance is the overall essential but whether such is achieved by intellectual methods of persuasion, magical suggestion, emotional reversal, or other methods of conversion is quite immaterial. Any ideological system that convincingly explains and rationalizes the causation of illness can be utilized as a therapeutic instrument."

P. E. C. MANSON-BAHR (*The Physical Background of Mental Disorder in Africans*, pp. 477–479) briefly indicates those acute or chronic infections which may be overlaid with psychotic or psychoneurotic symptoms which are relieved on physical improvement, and goes on to discuss pellagra and vitamin B deficiency, and acute or chronic infections of the central nervous system, which have a bearing on mental disorder. He notes that epilepsy is common in Africans, but the reasons for this are not understood.

C. G. F. SMARTT (*Problems and Prospects of Psychiatry in Tanganyika*, pp. 480–485) traces the growth of the institutions provided for treatment, and stresses the part played by social advancement in the incidence of admissions of senile and mentally defective patients. Diagnosis and treatment are rendered more difficult by the difficulties of language, but though facilities are still poor in relation to needs, progress is being made. He also stresses the background: "The rural African with his regulated life, in which every member of the group knows the whole social pattern of the group, lives a happy carefree existence. In spite of the disadvantages the mind of the rural African is probably protected rather than harmed by his primitive beliefs. His problems are mainly nutrition and the constant battle against physical disease. Today this remains mainly a public health problem rather than a mental health one. It is the urbanized African, as education and social advancement bring their heritage of anxiety and frustration, who is likely to present the mental health problem in the foreseeable future".

[This collection of papers constitutes a penetrating assessment of a society in rapid evolution; there is remarkable unanimity of opinion.] *Charles Wilcocks*

Sanitation

The order in this section is:—**General; Water and Swimming Baths; Sewage, Trade Waste and Refuse Disposal; Housing; Infestation; Atmospheric Pollution; Port, Ship and Aviation Hygiene.**

WATER AND SWIMMING BATHS

(Including the Bacteriology of Water Supplies)

HENNIG, K. & FRITZ, H. Fluor und Schilddrüse. **[Fluorine and the Thyroid Gland]** *Schweiz. med. Woch.* 1961, Jan. 21, v. 91, No. 3, 79–81. [17 refs.]

The undoubted value of fluoridation as a preventive of dental caries has nevertheless led to the fear that the ingestion of small amounts of fluoride over a period of years may have adverse effects particularly on the thyroid gland. The literature on the effects of fluoride on the thyroid function in man and animals, which is here shortly described and discussed, is conflicting. This conflict may, it has been suggested, be due to the great differences in dosage and type of compound of fluorine which have been used in the experiments.

Here reported are the results of the examination of 26 men aged 53–72 years (mean 59 years) who had been exposed to fluorine in the course of their work during a period of 6–37 years (mean about 19 years). X-rays showed fluorosis of the bony skeleton of slight to severe degree in most of these workers. All these men were submitted to tests of the basal metabolism, the serum cholesterol level and of thyroid function by means of

radio-iodine. The results of the tests are given in a table and are discussed. No evidence of deleterious action of fluoride on the thyroid was found, although it is clear that many of these workers must have ingested considerable amounts of fluoride in their years of work.

The authors consider that the daily dose of 1·0 mgm. fluorine which has been proposed for dental prophylaxis need not arouse any fear of adverse effect on the thyroid gland. *M. E. Delafield*

MARKARJAN, M. K., RYSHOW, N. V. & STANNIKOW, J. V. Sanierung von mit Botulinustoxin verunreinigtem Wasser. **[The Disinfection of Water Polluted with *Clostridium botulinum* Toxin]** *J. Hyg. Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 4, 385–9.

As there is no reference in the literature to methods for rendering water polluted with *Clostridium botulinum* toxin safe for consumption it was decided to investigate this subject. This paper contains a short account of the methods employed for making the sterile toxin solution for addition to the water which was then treated in a variety of ways before testing the remaining toxicity by intraperitoneal inoculation into white mice of which 1,200 were used in 115 experiments.

It was found that chlorine in a concentration of residual of 0·7 to 1·6 mgm. per litre was ineffective but that overchlorination at a residual of 9·6 to 13·7 mgm. per litre detoxified the water with a 30 to 40 minute exposure. Exposure to ultra-violet under the described conditions had no effect. Boiling the water for 10 to 15 minutes resulted in effective decontamination. Other experiments demonstrated that the toxin can be removed from water by activated charcoal or carboferrogel (*Karboferrogel-M*) either by shaking up for 5 minutes followed by standing for 30 minutes or by slow filtration through a 25–30 cm. depth of these materials. Some of the modern synthetic resin preparations (Ionexes) were also tested but were ineffective. *M. E. Delafield*

JOHANNESSON, J. K. **The Bromination of Swimming Pools.** *Amer. J. Pub. Health.* 1960, Nov., v. 50, No. 11, 1731–6. [22 refs.]

In the course of an investigation on the chlorination of sea water swimming pools it was found that the liberation of bromine from the naturally occurring bromide which is normally of a concentration of 70 p.p.m. caused the formation of bromamines as well as chloramines in the presence of nitrogenous matter from the bathing load. A study was then made of the chemistry and bactericidal action of these bromamines and the information obtained is presented here in a condensed form as it will be of value to those concerned in the bromine sterilization of bathing pools. Bromination of pools is used in the United States but extension of this procedure is limited by lack of knowledge of the behaviour of bromine in its reactions with ammonia and lack of methods to determine whether a residual of bromine is free or combined.

Sections of the paper contain chemical and physicochemical information on the hydrolysis of bromine in water with the formation of hypobromous acid, hypobromites and bromates ; and the conditions under which, in the presence of ammonia, bromamines are formed. The chemical reactions of the bromamines are described and there is a discussion of the phenomena of bromine " break point ". There are references to the literature on the bactericidal action of bromine and the author has shown that the bactericidal action of monobromamine on suspensions of *Escherichia coli* and *Streptococcus faecalis* is nearly the same as that of bromine. In a short description of analytical methods it is stated that the author's method of determining the type of bromine residual by amperometric apparatus is to be published elsewhere.

In the conclusions there is some discussion of the advantages of bromination over chlorination and it is considered to be " likely that the very strong bactericidal properties of the bromamines may be exploited by the use of a small combined bromide residual since there is no need to reach break point in order to achieve strong disinfectant properties in the bathing water ".

M. E. Delafield

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

KURLAND, T., FARO, S. N. & SIEDLER, H. **Minamata Disease. The Outbreak of a Neurologic Disorder in Minamata, Japan, and its Relationship to the Ingestion of Seafood contaminated by Mercuric Compounds.** *World Neurology.* Minneapolis. 1960, Nov., v. 1, No. 5, 370–95, 10 figs. [66 refs.]

This review shows that this degenerative disease of the brain is associated with mercury-containing effluent from a factory where mercuric chloride is the catalyst in the production of vinyl chloride from acetylene and hydrogen chloride [see also this *Bulletin*, 1959, v. 34, 71]. Laboratory animals developed the disease, which was similar to one produced by organic mercurials, when fed with Minamata Bay shellfish, whether autoclaved or not. Ashed residue, from which metals including Hg were volatilized, was not toxic. The Hg content of brain, liver and kidneys was elevated—as it was in patients. There was correlation between the Hg content of fish and the amount of fish required to affect the animals. The toxic agent was found in the hydrolysate following enzymatic digestion of fish : it was suggested that (in the living fish or other marine life) an alkyl Hg compound combined to form a protein complex, since the chloride would not affect the nervous system. Clinical and pathological findings are surveyed, and the differential diagnosis and published reports of poisoning by organic Hg compounds.

Large quantities of Hg were found in the mud of the

bay and effluent. The incidence of the disease increased with vinyl production and fell after a fishing ban in 1956. The bay effluent was closed in 1958, and another opened in the Minamata River. Maps show the distribution of 83 patients (no babies) affected from 1953 to 1960. Recent subjects include some who ignored the ban or fished at the river mouth, but also fishermen who lived along the sea coast. Emaciated fish, some with cataracts, have been observed swimming, in an abnormal fashion, from bay and river.

The problem does not exist in Galveston Bay, Texas. At a nearby plant, the vinyl is purified by distillation and Hg lost from the reactors dispersed as oxides high in the air. Hg was only found in a swamp near a spent catalyst holding basin. Industrial waste is controlled, tidal and drainage conditions are different, and so are dietary habits. In Minamata, Hg and other impurities are removed by washing into the effluent, and now a settling basin and a cyclator have resulted in almost all the Hg being removed from the washings which previously contained 300 gm. Hg each day. The spent catalyst was dumped near the river, but the Hg is now removed by distillation.

Recommendations are made which may aid in control of the disease or its prevention elsewhere. Unused ammunition, presumably containing Hg fulminate, was dumped at sea after the war. There is no indication that this was done at Minamata. 5 case-histories are given.

M. Patricia Fitzsimons

ATMOSPHERIC POLLUTION

DEPT. SCIENT. & INDUST. RES. **The Investigation of Atmospheric Pollution. Research and Observations in the Year ended 31st March, 1958. 31st Report.** pp. iv + 164, 5 figs. 1960. London: H.M. Stationery Office. [8s.]

As in previous years, this Report largely consists of tables summarizing the measurement of atmospheric pollution made by the 381 bodies—local authorities, industrial undertakings and other institutions—which cooperate with the Department of Scientific and Industrial Research in collecting data. These tables contain an enormous amount of information, for the measurements made with every instrument operated by the cooperating bodies are summarized separately. Where suitable the data are broken down by months, by seasons (summer versus winter), and by week-day versus week-end.

The tables are prefaced by a brief report of the Atmospheric Pollution Research Committee and by the report of the Director of Fuel Research on the investigation of atmospheric pollution. The latter report discusses very briefly the application of the Clean Air Act, which was just getting under way in the year under review, and goes on to consider the emission of pollution. In the country as a whole the emission of smoke fell by about 11% between 1955–56 and 1957–58, mainly because smoke from industrial sources fell by over 20%, but that of sulphur dioxide rose by 4%. In London the situation is much better, with a fall of 25% in smoke and of 6% in SO_2. For the whole country the average concentration of smoke in the air decreased steadily in the same period, roughly in step with the fall of emission. In contrast, the SO_2 in the air did not increase although emission did; the difference is attributed to the use of higher chimneys at large sources of SO_2. Pollution in the City of London and surrounding areas is considered in rather more detail.

Finally the work of the Fuel Research Station on the abatement of atmospheric pollution is outlined under the headings: Production of reactive domestic coke; Smoke elimination from boilers; Measurement of smoke; Combustion of fuel oil; Removal of sulphur compounds from flue gases; Exhaust gas from motor vehicles; Dispersal of chimney gases.

John Ellison

MARTIN, A. E. & BRADLEY, W. H. **Mortality, Fog and Atmospheric Pollution. An Investigation during the Winter of 1958–59.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1960, May, v. 19, 56–72, 3 figs. [13 refs.]

In the appendix to this report the number of deaths occurring on each day from 1st November, 1958 to 28th February, 1959 in the Greater London conurbation are tabulated for all causes combined and bronchitis and pneumonia separately. Mean measurements of atmospheric pollution recorded at 9 a.m. in respect of the previous 24 hours were obtained from 7 stations, "chosen to be as representative as possible of the County of London", and the appendix also shows for each day the amount of black suspended matter in mgm. per 100 cu. metres and sulphur dioxide (SO_2) in parts per 100 million. The deaths and pollution data are also shown on a time series graph. The appendix also includes daily assessments of the minimum visibility from the Air Ministry Roof in Kingsway. These assessments are based on a non-linear-scale from 1 (less than 22 yards) to 9 (more than 4,400 yards). These data, and other meteorological information not given in detail, are examined for relationships between the mortality variables on the one hand and the air pollution and weather variables on the other.

During the 120 days, fog (visibility less than 1,100 yards) occurred on 59 days and thick fog (visibility less than 220 yards) on 22 days. 6 periods of severe fog were recorded lasting 6, 3, 2, 4, 6 and 3 days and each was accompanied by increased air pollution, and 4 of these episodes resembled the "smogs" of 1952, 1956 and 1957 [this *Bulletin*, 1958, v. 33, 1158]. Each of the 6 fogs was associated with an increase in the number of deaths. The increases above what might have been expected from the general level of mortality ranged from about 70 deaths in the fog of 2nd-4th December to 230 in that of 26th–31st January. An examination of the peaks in the mortality and pollution graphs reveals a number of small coincident peaks; thus there were 34 days when the number of deaths from all causes increased by 20 or more over that on the preceding day and on 21 of these days the black

suspended matter increased by more than 20 mgm. per 100 cu. metres and on 25 the SO_2 increased by more than 2.5 parts per 100 million.

A more formal analysis of the available data was attempted by methods of correlation. The effect of the seasonal trend in the mortality was eliminated by fitting a 15-day moving average to each of the 3 series and using for the correlation analysis the deviations of the observed number of deaths from the 15-day average line. These deviations are described as mortality indices. [No justification for the use of a 15-day moving average for this purpose is given and the choice of this rather than any other type of moving average or method of curve fitting appears somewhat arbitrary.] Significant (at $P<0{\cdot}05$) correlation coefficients (r) were obtained between the mortality indices for all causes and the amount of black suspended matter on the same day ($r=0{\cdot}585$) and between the same mortality indices and the logarithm of the amount of black suspended matter on the same day ($r=0{\cdot}613$). A small significant correlation ($r=0{\cdot}266$) was found between the mortality indices and black suspended matter on the previous day, but this is possibly due to the dependence of successive days' measures of pollution because the authors show a significant correlation ($r=0{\cdot}550$) between pollution on one day with that on a previous day. A significant correlation between the mortality indices for all causes and the logarithm of SO_2 pollution also emerged ($r=0{\cdot}520$), but the logarithm of SO_2 is also highly correlated with that of black suspended matter on the same day ($r=0{\cdot}894$). The multiple correlation between the mortality indices and the two pollution measures is only ($r=0{\cdot}62$). The bronchitis mortality indices gave correlation coefficients which were significant with the logarithm of the amount of black suspended matter on the same day ($r=0{\cdot}411$) and the logarithm of the SO_2 pollution on the same day ($r=0{\cdot}323$), but no significant coefficients were detected when the pneumonia mortality indices were considered.

Visibility was negatively correlated with mortality from all causes (*i.e.* as visibility decreased mortality increased) the relevant coefficient being of the order of $r=-0{\cdot}5$, but there was also a high significant negative correlation between visibility and logarithm of black suspended matter ($r=-0{\cdot}783$) and the multiple correlation between the mortality index on the one hand and both minimum visibility and logarithm of black suspended matter ($r=0{\cdot}59$) suggested that no great contribution to the association with mortality by either of these variables independent of the other could be detected. Other meteorological variables (daily mean temperatures, humidity and barometric pressure) showed no material association with mortality.

[With the data tabulated many simple and multiple correlation coefficients could be calculated and it would have been of interest to know what factors the authors considered in making their selection in so far as bronchitis and pneumonia deaths and the weather were involved. The significance of a correlation coefficient involving 2 time series is complicated if serial correlations are present in both variables and consequently it would be of interest to know more about the serial correlations of each variable. These were presumably examined as one such correlation is quoted for black suspended matter.] [See also this *Bulletin*, 1959 v. 34, 796.] *E. A. Cheeseman*

Occupational Hygiene

The order in this section is:—**General; Occupational Physiology; Occupational Diseases (Dust Diseases, Poisoning, Skin Diseases, Others); Occupational Psychology; Heating, Lighting and Ventilation.**

GENERAL

LIDDELL, F. D. K. **The Measurement of Occupational Mortality.** *Brit. J. Indust. Med.* 1960, July, v. 17, No. 3, 228–33.

The comparison of the mortality experienced by different occupational groups of the population is best achieved by calculating age-specific death rates for each occupation so that mortality experienced by sub-groups of similar age can be compared. In this way differences which are apparent at some ages but not at others can be detected and interpreted intelligently with regard to age influences not only on the mortality comparison but also on the quality of the data about population, occupation and death. This is not always done and mortality experiences are often "standardized" for age and various "single figure" indices, here called "standardized mortality ratios" (SMR) have been proposed. The indices discussed in this paper have in common the characteristic of being weighted averages of age-specific mortality ratios. In this sense an age-specific mortality ratio for a given occupation at a given age-group is the death rate in that age-group and occupation divided by the death rate in the corresponding age-group for all males where the "all males" experience is used as a standard. The essential difference between the four single figure indices considered in this paper is the system of weights applied to the age specific mortality ratios.

The indices considered are as follows and the methods of calculation are given in the paper with particular reference to the Registrar General's data on occupational mortality 1949–53 in England and Wales. (1) SMR (direct) is usually known as the comparative mortality figure and is an average weighted according to the age distribution of deaths experienced by all males. (2) SMR (indirect) is usually known as the standardized mortality ratio without qualification and has been used extensively by the

Registrar General in occupational and other studies since 1931. Weighting of the age-specific mortality ratios is according to the age distribution of deaths expected in the occupation had its population experienced in each age-group the same mortality as that in the corresponding age-group for all males. (3) SMR (inverse) recently proposed by KERRIDGE [this *Bulletin*, 1959, v. 34, 8] to meet an unusual situation which in occupational studies would correspond to the age distribution of the occupation, and consequently its age-specific rates, being unknown. In this the weighting system is equivalent to the age distribution of the population in the occupation. (4) SMR (new) is proposed by the author and results from the use of the age distribution of the population of all males as the system of weights.

The kind of results which can arise if all four SMR are calculated for the same occupational groups is typified by quoted values for hewers and getters as one occupational group and other coal-miners as another. The SMR (direct) are 157 for the former and 96 for the latter, the SMR (indirect) are 153 and 96, the SMR (inverse) are 132 and 105, and the SMR (new) are 135 and 106.

Recent work by REID [*ibid.*, 446] and the author and his colleagues [*ibid.*, 1958, v. 33, 1143] has emphasized the sources of inaccuracy in statements of occupation and the difficulties of interpretation which arise through the use of the last occupation followed by a deceased person in official analyses of occupational mortality. They showed that errors were particularly likely in the older age-groups. Thus the SMR (direct) and SMR (indirect) which give relatively more weight to the older age-groups than do the SMR (inverse) or SMR (new) are probably less reliable than the two newer methods in dealing with causes of death and occupations with heavy mortality at the older ages. Nevertheless, no average alone can hope to adequately describe a complete distribution of age-specific mortality ratios and it is to be hoped that the need for such "single figure indices" will seldom arise in the future. *E. A. Cheeseman*

MCGREGOR, D. **Sickness Absence among Forestry Workers in the North of Scotland, 1958.** *Brit. J. Indust. Med.* 1960, Oct., v. 17, No. 4, 310–17, 3 figs.

This is an analysis of the records of sickness absence of 4 days or more of 1,115 forest workers in the highlands of Scotland during 1958. These records are compared with those of 750 men in the outdoor construction gangs of the Post Office telephone districts of Aberdeen and the West of Scotland. The results of the analysis are set out in a number of clear figures and tables with 2 detailed appendices on absence from classified sickness and accidents.

Among the forestry workers there were 270 on the established list and so entitled to retirement pension. There is a higher proportion of older men in this class than in the unestablished class yet the sickness record of the established is generally better than that of the unestablished except in respect of cardiovascular disease, rheumatism and arthritis. The most important cause of absence from work in forestry workers was accidents off duty which accounted for more days lost than did accidents on duty. Second in importance on the list of absence causes were "back troubles" which are discussed for "observations about them are still not collected in a form in which their natural history can be studied" since a variety of "diagnoses" which do not necessarily represent different diseases appear on medical certificates.

Of interest is the finding that the incidence of bronchitis in forestry workers is much less than in the male working population at large.

There is some description of the work and conditions of work of the forestry workers and that of the men in the telephone gangs. The main difference between them is that the latter live in an urban area although they may be away from home in lodgings for long periods of 3 or 4 months and sometimes more than a year. There is, however, a broad similarity in the health hazards of the working environment of the 2 groups of men and it is difficult to determine the factors which operate to bring about the differences in health absence experience. The main differences were that, when adjustment is made in the age constitution of the 2 groups, sickness absence for bronchitis, cardiovascular disease, and peptic ulcer and gastritis was less in the forestry group than in the telephone construction group. *M. E. Delafield*

KÖHEGYI, I., KUN, L. & MÉRO, E. Die Beziehungen zwischen der Betriebsmorbidität und den Arbeitsverhältnissen. **[Relationship between Industrial Morbidity and Conditions of Work]** *Arch. f. Gewerbepath. u. Gewerbehyg.* 1960, v. 18, No. 3, 258–85, 8 figs. [17 refs.]

This is a long detailed paper in which the morbidity statistics for 1954–56 of 7,717 workers in 4 industries (leather, coke, porcelain and machine factories) in Pécs, Hungary are analysed.

The illnesses suffered were grouped under the headings of (1) skin, (2) respiratory system, (3) digestive organs, (4) circulation and blood-forming organs, (5) urino-genital system, (6) "colds", (7) infections, (8) motor organs; (9) eyes, ears and nose, (10) accidents and (11) other diseases.

Tables and detailed description with discussion give the results of the comparative analysis. The 18 tables of numerical data cover (1) the percentage distribution of the different illnesses causing absence from work in all the workers, (2) the proportion of illnesses in men as compared with women, (3) illness by age in the sexes, (4) number of work days lost for the 11 illness groups, (5) duration of illness and number of cases of the different illnesses in the 4 types of factory and (6) seasonal distribution and other matters.

There is a long summary. *M. E. Delafield*

TILLMANN, R. Auswertung der Reihenuntersuchung bei Arbeitern mit Pressluftwerkzeugen. **[Routine Examination of Compressed-Air Workers]** *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1960, Dec., v. 6, No. 12, 790–96.

In East Germany the law requires that all workers with compressed air be given at least an annual routine examination by methods which are stated.

From his experience of dockyard workers the author of this paper makes proposals for the amplification of the legal requirements as regards examination which he considers would be useful in a variety of ways.

The proposals are here set out in detail with tables and forms to be used for the recording of information. Included are the questions to be asked to ascertain the past and present history of the worker, the details of the findings of X-ray examination and audiometer testing and the special methods of their recording.

Although it is realized that these forms for recording may appear at first sight to be an extra burden on the examiners, the author considers that this will not be found to be the case. Furthermore these forms from all industries where compressed air workers are employed would if collected at some central place constitute valuable material for comparative studies.

It is emphasized that these proposals are not to be regarded as the last word but they are presented as a basis for discussion. *M. E. Delafield*

RAYMOND, V. Arthroses baro-traumatiques. [**Arthroses in Decompression Sickness**] *Arch. Malad. Professionnelles.* Paris. 1960, Oct.–Nov., v. 21, Nos. 10/11, 609–21, 1 fig.

Arthroses of the shoulder and hip attributed to decompression sickness were included in the list of notifiable occupational diseases in France on the 9th February 1949 following a recommendation from the Industrial Hygiene Committee of the Ministry of Labour. Subsequently the number of registered cases of this affliction in caisson workers and divers rose steadily, reaching a peak incidence in the years 1952, 1953 and 1954 but afterwards stabilizing at a level of 7 new cases a year. Altogether, 111 cases have been notified in the 10-year period after 1949 but it has not been possible, for various reasons, to relate the incidence to the population at risk.

The authors have studied 30 of the notified cases, 27 caisson workers and 3 divers and here report their findings in detail. Their findings differ in no respect from those reported by other investigators in the past. They express the opinion that arthroses in decompression sickness are similar radiologically and otherwise to the degenerative arthroses, but develop at an earlier age, and that they result from the repeated attacks of minor pains ("niggles") to which caisson workers and divers are so subject. Bone and joint changes in decompression sickness may be due to air emboli in the bone cavities and in the terminal arterioles of the head of the femur and of the humerus but the alternative suggestion put forward in this paper is that of changes in the spinal cord and in the fine branches of the peripheral nerves due to air emboli. *P. J. R. Challen*

COLES, R. R. A. & KNIGHT, J. J. **Auditory Hazards in a Diesel Engine Test House.** *Ann. Occup. Hyg.* London. 1960, Nov., v. 2, No. 4, 267–73. 4 figs.

Noise levels measured at working positions inside a diesel engine test-house ranged from 102 to 116 db., and were in excess of accepted damage risk criteria. Audiometric tests on 6 men who had been working regularly in this location over a mean period of 3½ years, showed that all had hearing losses of 45–60 db. in one or both ears at 3, 4 or 6 kc. per second. The occurrence of temporary threshold shift confirmed the hazardous nature of the noise exposure. *D. E. Hickish*

DEPT. SCIENT. & INDUST. RES. Building Res. Station. **The Lighting of Factories** [KEYTE, M. J. & GLOAG, H. L.]. *Factory Building Studies No. 2.* 1959, pp. iv + 28, 30 figs. London: H.M. Stationery Office. [3s. 6d.]

This booklet contains an account of the principles of good lighting followed by a discussion of practical applications which is well illustrated. The principles hold for natural as well as for artificial lighting. They include properly relating the working illumination level to the characteristics of the work-objects that have to be visually discriminated. A table covering a variety of types of work is given to show what level of illumination is considered desirable for each type. In addition, factory lighting should be achieved without being glaring, and the general distribution of light should be such as to create a satisfactorily but not monotonously bright environment. The illuminant should be chosen to give acceptable colour rendering for the particular purpose. The effect of different methods of fenestration on the distribution of daylight in factory buildings is explained with the aid of 16 diagrams. Practical methods of artificial lighting are discussed briefly, with photographic illustrations, and some useful lamp data are tabulated. Other aspects of factory lighting discussed are the design of artificial lighting for parts of factories where it must be used always to supplement continuously inadequate daylighting, or be used permanently as a complete substitute for natural lighting in windowless buildings.

The booklet should serve its intention of aiding factory managements to assess their lighting requirements well enough to brief their architects and lighting engineers in more than the most general terms. It should also be of interest to industrial medical officers, welfare supervisors and others concerned with industrial efficiency. *H. C. Weston*

MICHELI, F. Malattie ipertensive nel campo del lavoro. Considerazioni sulla loro profilassi. [**Hypertensive Diseases in Workers with reference to its Prophylaxis**] *Med. d. Lavoro.* 1960, Nov., v. 51, No. 11, 714–20. [Numerous refs.] English summary.

The works medical officer should anticipate and prevent or control hypertensive disease and he should aim at discovering any workers who may have a liability or predisposition to high blood pressure. Such individuals should not be allowed to take, or remain in, jobs which are known to cause high blood pressure and possibly lead to cardiovascular disease.

The author believes that a liability to hypertension can be detected if present, even in relatively young persons, if family history is carefully studied, blood pressure readings are correctly interpreted and the physical and psychological pattern of the individual is

considered in each case. Such aids as the "Cold Pressor Test" of HINES and BROWN may be of value in diagnosis (*Ann. Intern. Med.*, 1933, v. 7, 209).

Chronic industrial poisoning from lead, mercury and carbon bisulphide involves the cardiovascular system, and some other industrial poisons—such as carbon dioxide, nitro-glycerin and nitroglycol—may lead or contribute to the development of coronary disease. Chloride derivatives like carbon tetrachloride and dichlorethane, chromates, oxalates and some other chemicals used in industry may give rise to acute and chronic poisoning with eventual renal insufficiency, blood pressure changes and involvement of the cardiovascular system. An occupation which has to be carried out in a hot atmosphere is liable to upset the water and mineral exchanges of the body and may have cardiovascular repercussions. *J. Cauchi*

See also p. 470, FUCHS [**On the Problems of Occupational Leptospirosis in So-Called Dirty Professions.**]

CROTON, L. M. **Recent Developments in Techniques of Artificial Respiration.** *J. Inst. Sci. Technol.* London. 1960, Apr.–June, v. 6, No. 2, 5–13, 10 figs. [13 refs.]

In this article the author reviews the evidence presented before the National Academy of Sciences and the National Research Council of the U.S.A., which led to the adoption of SAFAR'S method of mouth-to-mouth breathing as the best technique for manual artificial respiration. Further evidence is quoted to show that teenagers can perform this method without undue fatigue. Mention is made of several types of plastic airway that have recently been placed on the market for use by first-aid workers and there are illustrations of the training mannikin produced by Messrs. AMBU International of Copenhagen.

[See this *Bulletin*, 1960, v. 35, 225, 338, 339, 340.]

T. O. Garland

COLE, D. S. & WATT, W. J. **Cardio-Respiratory Resuscitation.** *New Zealand Med. J.* 1960, Aug., v. 59, No. 336, 367–75, 3 figs. [32 refs.]

The subject is discussed in two parts.

1. *Rescue Breathing and Artificial Respiration*

Here the method advocated is that commonly known as mouth-to-mouth breathing, where the emphasis is on establishing a patent airway in the victim and blowing expired air from the rescuer into the lungs. The main arguments given for this method are taken from the work of SAFAR, and there are some useful diagrams added to the description of his techniques.

2. *Cardiac Resuscitation*

In the Auckland Hospital Board's institutions 20,000 anaesthetics were given during 1959 and in 20 deaths which occurred among these cases cardiac massage was attempted. 17 of these cases, 12 of them in children under 10 years, are subjected to a close analysis of the factors leading to death and the reasons for failure to resuscitate the heart. Delay in taking the decision for the necessary drastic procedure is given as the chief reason. The authors particularly deplore the time spent in confirming the diagnosis by further investigations after the absence of pulsation in the carotid artery or abdominal aorta has been noted.

Full details of the technique recommended for massaging the heart are given and there is some discussion on the use of an electrical defibrillator and of the drugs adrenaline, calcium chloride and procaine in the management of cardiac arrest. *T. O. Garland*

OCCUPATIONAL PHYSIOLOGY

YAGLOU, C. P. **Effect of Geographical Origin on Performance in Heat.** *Arch. Environment. Health.* Chicago. 1961, Jan., v. 2, No. 1, 1–8, 5 figs.

The effect of geographical origin on the capacity for work in the heat was studied by comparing the physiological cost of walking (a) in a group of young men from southern Florida, and (b) in a similar group of northerners transported to Florida from New England. All the subjects were college students.

The experiments were carried out in July and August. In July the rate of walking was 3 miles an hour, and in August it was 3½ miles an hour. 2 work schedules were used:—(a) 3 50-minute walks in the sun with 10-minute rests in the shade; and (b) 1 150-minute walk in the sun followed by a 30-minute rest in the shade. The results obtained with the 2 schedules were practically identical. Heart rates, rectal temperatures and clothed-body weights were observed in all experiments, and oxygen consumptions were measured 2 to 4 times a week. The meteorological observations included measurements of the dry- and wet-bulb temperatures in the sun and in the shade, of the solar radiation on a horizontal plane and of the reflected radiation from the terrain, globe thermometer temperatures, ground and "sky" temperatures from observations with a radiation thermopile, and wind speeds. As a single index of warmth the wet-bulb-globe temperature (WB-GT) was used. Air temperatures ranged from 79° to 89°F., wet-bulb temperatures from 74° to 79°F., wind speeds from 2 to 13 miles an hour, and WB-GT values from 77° to 85°F.

The speed of acclimatization differed in the 2 groups. The northerners initially had higher heart rates and body temperatures during work than did the southerners, and they required at least 5 days to reach a semblance of acclimatization, compared with 3 days for the southerners as a group. Some of the southerners required little or

no acclimatization. During periods of cool, rainy weather the northerners lost acclimatization faster than the southerners even though the tests were continued under cover.

After acclimatization the southerners had a slightly lower metabolic rate during work, a distinctly lower rate of sweating, and a smaller rise in rectal temperature and heart rate.

As a measure of the total thermal strain of walking in the heat an empirical index was calculated by multiplying the rate of evaporative sweat loss by the increments in body temperature and heart rate. According to this index the physiological cost of walking was 40% greater for the northerners than for the southerners at a WB-GT of 79°F., and 70% greater at a WB-GT of 84°F. *Thomas Bedford*

OCCUPATIONAL DISEASES

BAADER, E. W. **[The Clinical Basis of the 46 Notifiable Occupational Diseases].**

This book was reviewed on p. 417.

SCHLIEPHAKE, R. W. Stand der Entwicklung eines röntgenographischen Routineverfahrens zur Quarzbestimmung in Grubenstäuben des Steinkohlenbergbaus. **[The Present Stage of Development of an X-Ray Diffraction Routine Method for Measuring the Quartz Content of Airborne Dust in Coal-Mines]** *Staub.* Düsseldorf. 1961, Jan. 2, v. 21, No. 1, 1–5, 3 figs. [14 refs.]

In routine dust control in coal-mines in Germany 2 types of samples are taken, ordinary samples, evaluated by light scattering, and by determination of non-coal proportions on conimeter spots, and special samples for determination of size distribution and quartz content. The paper describes an X-ray method for routine quartz determinations developed in response to the need for more reliable results than are given by microscope evaluation. The method had to be quick and to need little material.

The method used requires a sample weight of 7 mgm. of dust ash. It uses an X-ray diffractometer, Cobalt $K\alpha$ radiation and a scintillation counter as detector. In order to get sufficient intensity, a curved receiving slit of 23 mm. height and 0·6 mm. width is used. Peak heights are measured on the quartz line at 1·81 Å, and the region of $2\theta = 56{\cdot}5 - 60{\cdot}5°$ is recorded. No absorption corrections are made in general. Errors due to absorption are likely to be largest in the presence of calcite and haematite and as lines from both would be recorded appropriate corrections could be made. No allowance for particle size is made either but as the calibration is based on actual mine dusts and on comparisons with quartz of similar size (<3 microns and 3–8 microns) this is said to be permissible.

A table shows very good agreement between quartz determinations by this method and by a chemical (phosphoric acid) method. 2 graphs show that the confidence limits of the correlation between X-ray and chemical results are closer when the particle size is restricted to a narrower size range.

10 determinations on one sample with 10% quartz show a range of values approximately between 9 and 10%. Various errors are considered theoretically, and the chief sources of error are found to be inaccuracies in determining the background and the numbers of diffracting quartz particles. Both theory and practice show a standard error of 6%, *i.e.* ±12% for a single determination. *G. Nagelschmidt*

MARASAS, L. W. & HARINGTON, J. S. **Some Oxidative and Hydroxylative Actions of Quartz: their Possible Relationship to the Development of Silicosis.** *Nature.* 1960, Dec. 31, v. 188, 1173–4.

After reference to previous observations of WEYL [this *Bulletin*, 1951, v. 26, 912] on the oxidative power of fractured surfaces of quartz or silica gels the authors describe new experiments in this field. They found that shaking 1 gm. of quartz with 5 mgm. of proline for 30 minutes produced a small amount of hydroxyproline, equivalent to the effects of 2 or 3 mgm. of hydrogen peroxide. Coarse quartz had less effect than fine quartz. A number of other similar reactions (oxidation or hydroxylations) are also described. All these are believed to be catalytic reactions in which oxygen from the air is used. This is followed by speculations in how this effect could be used to explain the development of silicosis. *G. Nagelschmidt*

MINISTRY OF POWER. **Pneumoconiosis in the Mining and Quarrying Industries. Digest of Statistics, 1959.** pp. iv + 19. 1960. London: H.M. Stationery Office. [3s. 6d.]

The Digest of Pneumoconiosis Statistics covers only the industries involving mining and quarrying and of these coal-mining is by far the largest. The introduction to the Digest warns us that rises in certification rates should not necessarily be taken as indicating that the prevalence of the disease is increasing. The figures presented are almost meaningless unless one consults the Digests of previous years. The information given refers to certifications by the Silicosis Medical Board of cases under the Workmen's Compensation Acts and the Pneumoconiosis and Byssinosis Scheme, and to diagnoses made under the National Health (Industrial Injuries) Act. In the course of time, the first two of these will disappear. The scope of the Workmen's Compensation Act is now practically limited to workers applying to return to the coal-mines, and there are now fewer of these, and

to death claims which are also decreasing. The pneumoconiosis and byssinosis figures have probably reached the peak as far as disability claims are concerned; the awards in force on 31 October, 1959 for total disablement have been diminishing over the past 5 years.

The National Insurance (Industrial Injuries) will provide the figures for the future showing at least the awareness of the disease, if not of its true incidence. In coal-mining cases the number of claimants (7,908) was very nearly the average for the previous 4 years and we may hope that this is about the limit. Of the 3,523 cases certified, 87 were under 35 years of age. As most of these have had less than 20 years exposure, it would appear that there are some failures of the dust preventive campaign in that period. Of some interest is the fact that 44 certificates of suspension were issued because of pneumoconiosis with tuberculosis. This proportion (1·2%) has steadily declined during the past 6 years as one would expect from the national figures. The other mining and quarrying industries are small in comparison with coal-mining; their association with tuberculosis in some cases is more definite. In tin-mining (1 in 8), slate-mining (2 in 15), slate-quarrying (5 in 20) and refractories (1 in 22) this association is clear and can be shown also in the figures for the previous 4 years. Tuberculosis is still a factor to be considered in coal-mining and in these industries. *Charles L. Sutherland*

FAY, J. W. J. & ASHFORD, J. R. **The Study of Observer Variation in the Radiological Classification of Pneumoconiosis.** *Brit. J. Indust. Med.* 1960, Oct., v. 17, No. 4, 279–92, 3 figs.

Two of the objectives of the National Coal Board Field Research are (1) to express the prevalence of pneumoconiosis at 25 selected collieries in terms of its various stages of severity as measured by radiological examination, and (2) to investigate the progression of pneumoconiosis at these collieries also in terms of the radiological examination. It is of vital importance that the readings of the chest radiographs should be subject to checks of their accuracy and consistency. "Models" have been designed for this purpose. In the Field Research two doctors have been responsible for the readings. Each film is read 3 times, twice by the medical officer responsible for the survey and once by the other medical officer. If the 3 readings agreed, the reading was taken as the "definitive" classification. In case of disagreement, the film is classified by joint discussion. Films are divided into categories 0, 1, 2, 3, for simple pneumoconiosis and 4 (Cat. A) and 5 (B C D) for complicated pneumoconiosis.

The first model, the Pij is based on the assumption that there exists a "true" category associated with each film; this true category is defined as the opinion which would be obtained most frequently in a long series of joint readings by the 2 observers in consultation. If an observer is examining a film belonging to a true category 0, it is assumed that the chance of his reading it as category 0 is a constant, Poo, depending on his performance at the time of reading and the batch of films concerned. When a film is near the boundary of a category, it is more likely to be read in either the higher or lower category, so that the probability of error will vary according as to whether the film is on the borderline between 2 categories. This model is intended to refer only to the study of "average" effects based on a large number of films representing complete colliery populations and should not be extended to cover any particular film.

The "Improved" Model is concerned only with simple pneumoconiosis. Each radiograph may be regarded as representative of a unique degree of abnormality which may be considered as the true abnormality of the film. For any given film, the true abnormality value must be located at some point on a continuum or abnormality scale which covers the whole range of simple pneumoconiosis.

The abnormality scale of the ordinary classification, though not invalid, is not a desirable one. A scale of abnormality must be chosen so that, whatever the true abnormality value of a film, the observer's readings will be distributed about this value with constant bias and variability at all points along the scale. For practical purposes the readings are made in terms of 4 categories, and the scale of measurement is made by selecting suitable positions for the category boundaries. The boundaries between categories 0 and 1 may be chosen as 0, that between categories 1 and 2 as 1; the boundary between categories 2 and 3 has to be calculated, it is 2–12.

Some of the applications of this model are described. This improved model gives a realistic representation of the actual mechanism of the reading process. It can be applied to any particular film, provided the distribution of reading errors is known. One objection to this model is the extent of the computations required to analyse the results in a satisfactory manner. The fact that it applies only to simple pneumoconiosis is stated to be a drawback [but surely the classification of a simple pneumoconiosis along the range of abnormality from 0 to 3 is the most important reading for practical purposes]. *Charles L. Sutherland*

ASHFORD, J. R. **The Classification of Chest Radiographs for Coalworkers' Pneumoconiosis. A Study of the Performance of Two Readers over a Period of Six Years.** *Brit. J. Indust. Med.* 1960, Oct., v. 17, No. 4, 293–303, 1 fig.

The Field Research of the National Coal Board have just completed the initial round of 25 collieries, and follow-up examinations at 5 collieries. The 2 readers of the radiographs at first made 3 readings in all of each film, 2 by one doctor and the third by the second doctor: this was modified in the last 2 collieries in the first round and in the second round, so that the definite classification was obtained on a single reading by each observer and on a joint discussion in disagreements.

The consistency of readings depends on the amount of abnormality in the batch of films as well as on the standards of the observers. There is a wide variation in the prevalence of pneumoconiosis in the selected collieries. The consistency of duplicate readings by an observer was gone into in detail and it was found that the standards of a single observer vary in time. The readings of each observer were then compared with the definitive readings. The amount of agreement increases

with the proportion of normal films. A major feature of the analysis is the tendency for the magnitude of reading errors to increase with increasing amounts of abnormality in the batch of films. Definitive readings are subject to appreciably less error than any single set of routine readings. The method of joint discussion provides a satisfactory way of measuring the prevalence of radiological pneumoconiosis. In view of the variation in individual reading levels it is suggested that the number of readers be increased. *Charles L. Sutherland*

FINULLI, M. & BELLINI, F. La distribuzione topografica degli addensamenti nella silicosi confluente. [**The Topographic Distribution of Massive Conglomerate Lesions in Silicosis**] *Med. d. Lavoro.* 1960, Nov., v. 51, No. 11, 705–13, 2 figs. [21 refs.] English summary.

The authors have studied chest X-ray pictures from 800 patients affected with confluent silicosis; ages varied from 40 to 60 years or more and duration of exposure to the hazard ranged from 5 to 20 or more years. The work of 467 had been in mines.

When the confluent patches were on one side only the right chest was twice as often involved as the left; the upper lobes were most commonly affected. Upper lobe lesions were seen 3 times as often on the right side as on the left.

Half the patients with bilateral lesions showed these to be symmetrically sited. In these cases, too, the upper lobes were most commonly affected.

Where an active or open tuberculous condition had supervened no significantly higher frequency was noticed on either side of the chest; the lesions still tended to be most prevalent in the upper lobes.

The findings are given in more detail in a number of tables and are graphically shown in 2 diagrams.

J. Cauchi

ONO, Y. & AKAGAWA, J. Über die Klinische Anwendung der Vergrösserungs aufname für die Röntgenologische Diagnose der Frühzeitigen Silikose. [**The Clinical Use of an Enlarged Image for the X-Ray Diagnosis of Early Silicosis**] *Bull. Yamaguchi Med. School.* 1958, Aug., v. 6, Nos. 1/2, 27–35, 8 figs. [20 refs.]

The authors have sought to improve the X-ray diagnosis of *early* silicosis. Instead of having the film in contact with the object to be radiographed they have put it at a distance of about 60 cm. from the under surface of the object. The image is correspondingly larger than that attained by direct contact. Preliminary experiments were done with a lung phantom made of solid paraffin and then observations were made on the human subject. The article is well illustrated by radiographs of patients suspected of early silicosis and, by comparing the contact films with those obtained at the increased distance, evidence is shown of the advantage of the method in the amount of detail observable in the lung tissue.

The authors point out that no advantage is claimed in the diagnosis of established silicosis but the value of the method is a real one if the detection of the early signs of the disease can thus be established. The working voltage was 80 KV., the current through the tube 18 mA., and the exposure times 0·3 to 0·4 seconds. *S. Russ*

KNAKE, Else & PETER, H. Fortgesetzte Untersuchungen über die Wirkung von oligomer gelöster Kieselsäure auf Gewebekulturen. [**Further Research on the Action of Oligomer Dissolved Silicic Acid in Tissue Cultures**] *Beiträge z. Silikose-Forschung.* 1960, No. 68, 37–49.

In an earlier paper, the authors were unable to show that silica in culture media in a strength corresponding to the blood level of silica in severe silicosis (10 γ/ml.) had any effect on the growth of portions of spleen and lung of rabbits. This result is different to that of other investigators. KIRSCH, *et al.*, [this *Bulletin*, 1960, v. 35, 859] tested the action of various strengths of silica solution on the swelling of mitochondria. The maximum effect was produced by solutions of between 50 and 100 γ/ml. while with weaker solutions (up to 5 γ/ml.) no connexion could be shown between the concentration of silica and its action. This last finding regarding the effect of low concentration agrees with the authors' findings. In the present research the earlier research was repeated with concentrations which Kirsch *et al.* found to be maximal. Details are given of the method of culture of spleen and lung tissue. To the fluid phase of the media of half of the cultures silica was added. The other half were controls. The silica solution was made up from Aerosil (Degussa) and the medium on analysis was found to contain round about 65 γ/ml.

The trial lasted 3 to 6 months. The histological examinations of the control cultures of the spleen are detailed, it is then stated that there is no difference with the cultures in culture media with added silica. A similar result is recorded with the lung culture. In both the test and control collagenous fibres developed equally. The action of the silica solution was not to promote either the development of fibres or their hyaline degeneration. The authors then discuss the solubility theory which their research tends to disprove.

Oligomer dissolved SiO_2 is not dangerous to cells from outside. It is the phagocytosis of quartz dust which causes the development of silicosis. Prophylaxis of silicosis may be possible if a means can be found to prevent the phagocytosis of dust.

Charles L. Sutherland

FURUKAWA, T. **Effects of Silica on the Multiplication of Animal Cells in Tissue Culture.** *Japanese J. Exper. Med.* 1960, Aug., v. 30, No. 4, 279–88, 6 text figs. & 4 figs. on 2 pls. [14 refs.]

A series of experiments were designed and carried out to observe the effects—if any—of silica on the multiplication of cells in tissue culture. 3 types of cell were used; fibroblasts from chick embryo hearts and lungs; tissue culture strains of fibroblasts; and fresh malignant cells of rat ascites hepatoma. Finely ground silica was added to each culture except controls. The amounts of

silica added were 0·0001, 0·001, 0·01 and 0·1 mgm. per ml. The cultures were maintained for 7 days and thereafter all counts were made. It was observed that silica caused multiplication only of the fibroblasts freshly derived from animal bodies. *A. Meiklejohn*

SAFFIOTTI, U., TOMMASINI DEGNA, A. & MAYER, L. **The Histogenesis of Experimental Silicosis. II. Cellular and Tissue Reactions in the Histogenesis of Pulmonary Lesions.** *Med. d. Lavoro.* 1960, Aug.–Sept., v. 51, Nos. 8/9, 518–52, 24 figs. [Numerous refs.]

[This is the second paper in a series to be published on histogenesis of experimental silicosis based on work carried out under the direction of Professor E. C. Vigliani in the University of Milan. The first communication (this *Bulletin*, 1961, v. 36, 327) described the methodology and terminology used in the work.]

Following recent observations on the role of immunological factors in the pathogenesis of silicosis the present studies were undertaken to provide a detailed analysis of the cellular and tissue elements which contribute to the histogenesis of fibrohyaline lesions as observed in the lungs and lymph nodes of rats following intratracheal injection of different dusts.

5 groups of 22 rats each were given a single intratracheal injection of the following suspensions:

Group I: 0·5 ml. of saline solution (controls);

Group II: 50 mgm. of Hematite dust in 0·5 ml. saline;

Group III: 50 mgm. of Quartz dust in 0·5 ml. saline;

Group IV: 50 mgm. of Cristobalite dust in 0·5 ml. saline;

Group V: 50 mgm. of Tridymite dust in 0·5 ml. saline.

The rats were killed at different intervals and the required histological material was appropriately stained. The findings in each group are described and the histological appearances illustrated by photomicrographs. Detailed findings are presented in a series of tables and graphs.

"A constant pattern of cellular reaction was observed in the histogenesis of the lesions induced by fibrogenic dust: phagocytosis of dust particles followed by necrosis of macrophages and subsequent proliferation of other histiocytes and fibroblasts, activation of plasmacellular elements, proliferation and degranulation of mast cells, development of a network of collagen fibers, deposition of hyaline substance.

"A close correlation between overall silicotigenic activity and single elements of cellular and tissue reaction was observed: necrosis of macrophages, plasma cells, mast cells, fibroblasts, fibrosis and hyalinosis all followed the same pattern at their onset in the lesions and they were also correlated with the extension of the lesions, while an inversely correlated pattern was found for the number of histiocytes.

"An interpretation of the role of each element of the reaction in the pathogenesis of experimental silicotic lesions is suggested on the basis of the endotoxic and immunological activity of substances released through necrosis of macrophages by the cytotoxic activity of crystalline free silica particles." *A. Meiklejohn*

SZABO, I., MODY, J. & SZEKELY, J. Les lipoprotéines sériques chez les animaux traités à l'acide silicique. [**Serum Lipoproteins in Animals treated with Silicic Acid**] *Med. d. Lavoro.* 1960, Nov., v. 51, No. 11, 672–7.

The English summary appended to the paper is as follows:—

"The action of silicic acid on serum proteins and lipoproteins has been studied using amorphous SiO_2 and quartz respectively. Protein and lipoprotein fractions have been determined by means of paper electrophoresis. The intraperitoneal injection of guinea pigs with amorphous SiO_2 resulted in a rise in the lipid fraction which was further increased if ACTH or DCA were administered simultaneously. The effect of cortisone on the other hand was only slight. When colloidal silicic acid was injected intravenously into dogs and rabbits, an alteration in protein pattern was observed similar to that noted in acute and subacute inflammations; a marked hyperlipaemia was also observed with a raised β/α ratio. These alterations were not affected by cortisone, but they were reversed by heparin. Amorphous SiO_2 and quartz powder administered to guinea pigs by intraperitoneal injection caused a rise in serum cholesterol."

OTTOWICZ, J. Wpływ niektórych hormonów sterydowych na doświadczalną fibroplazję wywołaną pyłem krzemowym. [**The Effect of some Steroid Hormones on the Experimental Fibroplasia produced by Quartz**] *Med. Pracy.* 1960, v. 11, No. 5, 369–76, 4 figs. [51 refs.]

The English summary appended to the paper is as follows:—

"The effect of testosterone, DOCA and estrogens on the experimental fibroplasia produced by quartz in the conditions of a pneumodermal pouch in castrated female white rats was investigated.

"After 5 days from the beginning of experiments the animals were sectioned and the thickness of the wall of each pneumodermal pouch was measured using the optical micrometer.

"The markedly intensified fibroplasia reaction was found in the wall of the pneumodermal pouch in animals maintained on testosterone (11 injections of 2·5 mg. per rat), the slightly intensified fibroplasia was also found in DOCA-group of animals (11 injections of 1·3 mg. per rat). The estradiol benzoate (10 injections of 1 mg. per rat) and the endogenous estrogens (control group of non-castrated females) in the same biological conditions inhibited the fibroplasia reaction and diminished the reactivity of the connective tissue to the fibrogenic action of quartz dust."

FELDMANN, A. Zur familiären Disposition sur Silikose. [**Familial Predisposition to Silicosis**] *Zent. f. Arbeitsmed. u. Arbeitsschutz.* 1960, Oct., v. 10, No. 10, 229–33, 1 fig.

This investigation was prompted by the publication of a paper by JACOB in *Zent. f. Arbeitsmed, u. Arbeitsschutz* (1959, v. 9, 15) on familial predisposition in

silicosis. The essential material consists of 391 families in which the father or eldest brother is taken as the central figure, and 262 of these were victims of silicosis. The first task was to find if the severity of the disease in the father or eldest brother was reflected in the other members of the family in an increased incidence. The incidence was found not to be greatly different whatever the degree of silicosis in the central figure. The number of cases in the families under consideration was then compared with the number found in the total employed population, and proved to be very similar. This was also the case with the proportion of silicotics in the employed group, who had no family connexions.

Jacob had compared the rapidity of development of silicosis in families according to a scale published by Beckmann *et al.* [this *Bulletin*, 1953, v. 28, 1061] and found the number increased in the higher degrees of rapidity. In the present study the greater number was in the slowly progressing type. This is in accordance with the frequency of slowly developing silicosis in the total population under investigation.

The author is of opinion that a familial predisposition to silicosis cannot be proved from his material. He believes that differences in the development of silicosis are due to other factors such as variations of dust inhalation owing to the variety of exposure at the working place, as well as certain peculiarities of the respiratory tracts. *Charles L. Sutherland*

Reichel, G., Ulmer, W. T. & Hertle, F. Untersuchungen über die Störung der Lungenfunktion bei obstruktivem Lungenemphysem und bei Silikosen verschiedener Schweregrade. **[Investigation of the Defect of Lung Function in Obstructive Emphysema and in Silicosis of Various Degrees of Severity]** *Beiträge z. Silikose-Forschung.* 1960, No. 68, 1–36, 5 figs. [57 refs.]

This is an attempt, by the use of a refinement of methods of investigation, to separate the effects on lung function caused by silicosis, from those caused by the most important form of emphysema, diffuse obstructive emphysema. Defects of lung function may arise from defective distribution. The ventilation may be normal but the blood supply to different alveolar areas may be altered—a circulatory defect. On the other hand, the blood supply may be normal but there may be obstruction in the airways or an unequal ventilation of alveoli —the obstructive form of ventilatory defect. A second form of ventilatory defect is produced by rigidity of the lung tissue—the restrictive type.

The apparatus used and the methods employed are fully described. 179 patients suffering from obstructive emphysema, who had never been exposed to dust, and 149 patients with silicosis were investigated.

The expiratory carbon dioxide concentration curve traced by the infra red absorption recorder was used as a means of distinguishing the obstructive from the circulatory and restrictive types of defect. The curve in the healthy person and in those with the circulatory defect both show a plateau.

In patients suffering from bronchitis and emphysema, the obstructive type was expected and it was found in 85% of cases. Except in very severe cases only 6% of the silicotic patients showed this obstructive type, and those who did so, had clinical signs of bronchitis. In normal persons the alveolar and arterial carbon dioxide pressures agree but in silicosis cases they may differ by 3 or 4 mm.Hg. according to the degree of silicosis. Even in the early stages of silicosis, lung function defects are present to the extent of 45% and this percentage increases with radiological progression. The circulatory defect is linked to an oxygen undersaturation due to disturbed perfusion of areas of alveoli, so that contact between blood and air is cut down.

Only in advanced cases of silicosis is there evidence of an obstructive ventilatory defect. This may be explained by concurrent bronchitis but the kinking and distortion of bronchial branches may play a part and may, in addition, favour the development of spasmodic or inflammatory processes in the bronchial tree.

Charles L. Sutherland

Sato, K. **[Long-Term Observation of Silicosis and Tuberculosis associated with Silicosis among Miners exposed to Dust of Moderate Silica Content, with special reference to Autopsy Findings]** *J. Sci. of Labour.* Tokyo. 1960, Sept., v. 36, No. 9, 480–95, 8 figs. (4 coloured on pl.). [11 refs.] [In Japanese.] English summary.

This is a report on radiological observations over a period of 7–10 years on 82 miners working in a gold-mine where the rock contained 37% of quartz. Increase in radiological findings was observed in 85% of the milder cases and 94% of the more severe. Tuberculosis was diagnosed in more than half of the advanced silicosis subjects, and the disease was almost always active; in the milder cases it was found in only one-quarter. The more severe the silicosis the higher the tuberculosis rate.

Chemotherapy on the usual lines was effective at first, but eventually the condition of all the patients deteriorated. The author therefore advocates chemoprophylaxis. At autopsy the tuberculous nodules were 5–10 mm. in size, with fibrosis, and they were found near the silicotic nodules. Cavities were found, but these did not show granulation or formation of epithelium.

Charles Wilcocks

Montesano, G. Prima esperienza sulla legge regionale della Valle di Aosta (12.11.1959 n. 5) per l'assicurazione contro la silicosi e l'asbestosi. **[Early Experiences with the Regional Law of Valle d'Aosta on Insurance against Silicosis and Asbestosis (12.11. 1959 n. 5)]** *Med. d. Lavoro.* 1960, Nov., v. 51, No. 11, 689–93. English summary (7 lines).

In Italy, national insurance against occupational silicosis was brought in during 1943, as a war emergency measure: benefits were made subject to a time limit of 15 years between the cessation of exposure to the dust hazard and the onset of silicosis, and there was also a time limit after which the rate of benefit could not be raised if the degree of disability increased. These time limits are hardly equitable under the circumstances.

The Regional Board of the Valle d'Aosta has now exercised the powers which local administrations are

given under the national law, and has introduced supplementary provisions of local application which abolish the time limits referred to above.

In this paper the author reports on 19 cases which he has dealt with during the year or so for which these more liberal measures have been available. He was unable to confirm the diagnosis of silicosis in 5 of the subjects. The age range of the other 14 was between 40 and 85 years. Exposure to the hazard had lasted between 3 and 25 years and had ceased between 16 and 28 years before the present examination. The degree of disability found was 21% to 100%.

The disease may take quite a time to become manifest and it may have set in long before the patient seeks medical advice; he may have retired from active work many years before and is unlikely to have been subject to any routine medical checks in the interval.

J. Cauchi

ZAHORSKI, W. Pylica u robotników zatrudnionych przy produkcji sztucznego grafitu. [**Pneumoconiosis in Workers of Artificial Graphite Plants**] *Med. Pracy.* 1960, v. 11, No. 5, 383–6, 4 figs. on 2 pls. [17 refs.]

The English summary appended to the paper is as follows:—

"Our results derive from about 5 years observation of workers in the carbon electrodes plants. The raw products, viz.: anthracite, oil coke and gas coke are there crushed and ground in a special mill. From the dust pollution examination results that in 1 litre of tested air (impinger) the dust particles amount exceeds 160 millions. 45 p. c. of these particles are of less than 1 μ of diameter. The content of SiO_2 in the dust is about 1·3 p. c.

"The radiological findings in workers engaged in this process after exposure of about 10 to 15 years show changes resembling those seen in coal workers pneumoconiosis. The pictures are characterised by an opacity of the granular patterns. The micronodular opacity is of 1—2 mm of diameter, and appears in the marked reticular structure. Specific fibrotic changes are often seen. No extensive massive shadows were observed."

CANCELLA, L. de C. A angiopneumografia na suberose. [**Angiopneumography in Suberosis**] *Gaz. Méd. Portuguesa.* 1960, May–June, v. 13, No. 3, 342–57, 5 figs. [Numerous refs.] English summary.

Suberosis is the pulmonary condition associated with prolonged exposure to cork dust. The author explains the technique of angiopneumography, which involves injecting contrast medicine into a vein, and taking 8 radiographs of the lungs at intervals of 1 second, with a final film at 12 seconds. The object is to follow the contrast medium through the pulmonary vascular tree.

He submitted 14 patients with suberosis to this procedure; they had worked for 11–45 years in atmospheres containing abundant cork dust, and the examination revealed marked extension of the phase during which the medium is visible in the arteries (normally 2–3 seconds), prolongation of the capillary phase (normally occurring at 4 seconds), and retardation and extension of the phase when the medium is in the veins (normally occupying the period 5–7 seconds after injection). From 7–8 seconds onwards the pulmonary vessels are normally free from contrast medium, but in one of the present series of patients the arterial and venous phases were seen overlapping at 12 seconds. Other phenomena were that the pulmonary artery was not increased in volume, there were enhanced visualization of the peripheral vessels and narrowing of the arteries in the lower zones, displacement of vessels and short circuits in the pulmonary vascular circulation.

In several patients abnormal angiopneumographic records corresponded with insufficiency of pulmonary ventilation as revealed by the other tests, and the author therefore commends the procedure for study of the pulmonary circulation time. *Charles Wilcocks*

KHOO, F. Y., TOH CHIONG HENG & LEONG HON KOON. **An Unusual Form of Reticulated Lung Disease, probably an Unidentified Type of Pneumoconiosis. A Preliminary Report.** *Singapore Med. J.* 1960, Sept., v. 1, No. 3, 96–8, 4 figs.

8 years ago—1952—physicians at the Tan Tock Seng Hospital, Singapore, observed among out-patients a number of cases in which the lungs showed similar abnormal radiographic appearances. These changes consisted of generalized reticulation associated with a "veil-like haze lending a ground-glass effect to the overall picture." Kerley's lines were also present. Apart from chronic cough the patients were all apparently in good health. The authors interpreted the radiographic appearances as signifying exposure to noxious dust or fumes. Proof of such an occupational risk was not found. Most were, however, opium smokers and Dr. Leong Hon Koon suggested that possible aetiological factor might be the inhalation of opium fumes and hence "opium lung". So far no opportunity has occurred for pathological studies so the authors wish readers to understand that this paper is simply a preliminary communication on work in progress.

A Meiklejohn

NOWACKI, J. Ołowica w fabryce akumulatorów. [**Lead Poisoning in an Accumulator Factory**] *Med. Pracy.* 1960, v. 11, No. 4, 223–46, 4 figs. English summary.

The author has studied the occurrence of lead poisoning in an accumulator factory in Poland between 1951 and 1957. 229 cases were observed in all, 94 of which occurred in a single year [the number of persons at risk is not stated]. A 3-fold rise in the number of cases occurred between 1953 and 1957, running parallel to and 1 year behind an increase in production which began in 1952. Figures are given for the annual number of cases in the different shops of the factory; a high incidence was observed in the foundry and the assembly and finishing shops. Most cases occurred in April and May, and there were considerably fewer in the winter months; in relation to duration of exposure most cases (97) occurred in the 3rd month, with a smaller peak between 10 and 12 months. The author considers that the occurrence of lead poisoning after 3 months of exposure

is a contra-indication to further work with lead, which in such cases leads to a severe form of lead poisoning which is refractory to treatment. 20 of 84 cases occurred in persons aged up to 26 years, and 29 in persons aged 26–35 years; consequently, from 1956 onwards persons younger than 25 were no longer employed, in view of their greater liability to develop lead poisoning. The results of clinical and laboratory examinations of 168 persons suffering from lead poisoning are given in detail.

D. J. Bauer

Saita, G. L'attività antitrombinica plasmatica nel saturnismo. [**Antithrombin Activity in Lead Intoxication**] *Med. d. Lavoro.* 1960, Nov., v. 51, No. 11, 694–704. [30 refs.] English summary.

Saita tabulates the laboratory results of a number of relevant tests, including the measurement of the coagulation time for estimating any antithrombin activity, which he has had carried out on specimens of blood and urine taken from, among others, 19 patients who were affected with chronic lead poisoning. The coagulation time was found to go beyond the upper limit of the normal range (for which he quotes another series of his findings) in 9 of the patients, and these showed other evidence of severe lead poisoning. He found that the coagulation time in these cases could be reduced to within normal limits by neutralizing the antithrombin factor in the blood plasma with protamine sulphate, or adsorbing the plasma on barium sulphate or heating the plasma to 56°C. or by using the blood serum alone and adding fibrinogen. For his technique, which he describes, the author has made use of an "antithrombin reagent" supplied by Hoffmanla Roche.

The author thinks that this increase of antithrombin activity indicates an impairment of the liver or pancreas functions or of both. The finding is constant in some cases of lead poisoning: in some others, coagulation time is found to exceed normal limits only during the acute phases of the condition (lead colic).

J. Cauchi

Carlin, C. E., Corigliano P., J., Gastañaga C., A. & Ochoa L., R. Riesgos ocupacionales en una planta de mercurio. [**Occupational Risks in a Mercury Plant**] *Salud Ocupacional.* Lima. 1960, Apr.–June, v. 5, No. 2, 3–8. English summary (3 lines).

This article refers to poisoning in a plant refining mercury on the western part of the central Peruvian Andes at the very considerable altitude of over 4,000 m. where Hg in the form of cinnabar is extracted by the open-cast method. Refining is done by distillation of the cinnabar at 600°C. About 130 tons are dealt with daily.

Air samples were taken by means of the "big impinger" from the mine, the refining plant, and the laboratory and at the same time 155 workers, 115 of whom were engaged in the actual mining, 18 in refining. and 22 in maintenance, were examined clinically, with special attention given to the nervous system; they had a 17 in. by 14 in. chest X-ray, and also a number of laboratory tests including blood counts, Hb, and urine examination with estimation of the urinary Hg.

The Hg concentrations in the air of the mine and of the laboratory were less than the MAC but in the refining plant concentrations ranged from a minimum of 0·04 to a miximum of 2·57 mgm. Hg per cu.m. (MAC 0·1 mgm.). None of the workers in the mine or in maintenance showed any evidence of Hg poisoning and in 56 of them urinary Hg averaged 0·024 mgm. per litre. By contrast in 16 of the 18 employed in refining the average urinary Hg was 0·224 mgm. per litre. 13 of these showed definite symptoms of mercurialism, with changes in the teeth and gums, albuminuria, abdominal, thoracic, and lumbar pain, headache, loss of weight and hypertonia of the lower limbs. Tremor was present in only 3. The average urinary Hg was 0·255 mgm. per litre. The systolic and diastolic pressures were greater in the 13 with symptoms than in either the 5 without definite symptoms [the 5 remaining refinery workers are all stated to have had changes in the teeth and gums, so that really all 18 in the refinery were affected] or any of the other workers.

The authors consider that the refinery was the evident source of poisoning, and that if the urinary Hg exceeds 0·25 mgm. per litre a figure which in any case is regarded as evidence of excessive exposure, the patients will show symptoms.

W. K. Dunscombe

Noe, Frances E. **Chronic Mercurial Intoxication. A Review.** *Indust. Med. & Surgery.* Miami. 1960, Dec., v. 29, No. 12, 559–64. [41 refs.]

This useful review emphasizes that recognition of potential hazards and preventive measures are of greater importance than diagnosis and treatment—especially in laboratories—because the insidious and non-specific symptomatology of Hg poisoning is such that an individual may be relatively symptom-free for a long time and then develop serious chronic illness. Nevertheless, symptoms, signs and diagnosis are described as well as toxic levels of Hg vapour, absorption and excretion, preventive techniques, particularly in handling the metal, ventilation and materials for equipment.

The vapour pressure of Hg at room temperature is nearly 200 times the maximum allowable concentration of 0·1 mgm. per m^3. Vapour can be detected at 8·5°F., and vaporization increases rapidly with rising temperature and with agitation of dust which microscopy may show to be mixed with otherwise invisible spilled Hg. Microscopy of cigarettes, tapped on the bench, or of pipes and tobacco may be equally revealing, and show a source of inhaling or ingesting Hg. During a day's work where the air contains only 15 μgm. per m^3 it is possible to absorb 72 μgm. Work should be done at arm's length, and paper work away from the bench. Filtering devices to clean Hg should be used under a ventilating hood, and where repeated operations are necessary with uncovered containers, the face velocity of the hood should be 150–200 linear feet per second. General ventilation should be of the down-draught type. Recirculating fans are dangerous. An increase in temperature of the Hg demands extra precautions. Containers should be covered. A film of water on Hg decreases vaporization but does not prevent it. Pans of

water should be placed under stopcocks or sources of leaks. If spilled, Hg should be wetted and picked up by means of suction-powered fine tipped glass tubing. Where spills cannot be avoided, clothing not to be taken out of the work area should be provided and specially laundered. Vacuum cleaning should replace the broom. These and other precautions are based on studies of chronic mercurialism made in industrial and scientific laboratories. *M. Patricia Fitzsimons*

PAGNOTTO, L. D., BRUGSCH, H. G. & ELKINS, H. B. **Treatment of Chronic Mercurialism with N-Acetyl-Penicillamine.** *Amer. Indust. Hyg. Ass. J.* 1960, Oct., v. 21, No. 5, 419–22, 1 fig.

Ethylene diamine tetra-acetic acid (EDTA) is not effective in mercury poisoning and dimercaptopropanol (BAL) by parenteral administration is effective only in the acute disease. Recently it has been shown that penicillamine (β,β-dimethyl cysteine) by mouth increases the elimination of metals such as copper and it has been suggested on the basis of animal studies that N-acetyl-penicillamine might be effective against mercury poisoning. The authors report their experience in the treatment of 2 cases of chronic mercurial poisoning, 2 workers with a moderate mercury exposure but no evidence of mercurialism, and 1 case of lead intoxication with this compound. The original should be consulted for clinical details, and for the tabulated data on mercury excretion in the urine following treatment. The drug was given in doses ranging from 1 gm. daily for 7 days to 3 gm. daily for 3 days. Other investigators have found a 10- to 100-fold increase in plutonium excretion during administration of EDTA and a 10- to 40-fold increase in lead excretion with the same drug [this *Bulletin*, 1954, v. 29, 833]. In this instance the case of lead poisoning showed a 2-fold increase with acetyl-penicillamine and a significant increase in the excretion of mercury was found although less than 2-fold.

The authors conclude that their limited experience is not sufficient for them to express an opinion on the efficiency of acetyl-penicillamine if used on a long-term basis in removing large amounts of retained mercury or on its effects on the clinical picture of acute mercury poisoning. *P. J. R. Challen*

SUZUKI, Y., NISHIYAMA, K., DOI, M., HIROSE, T. & SHIBATA, H. **Studies on Chronic Manganese Poisoning.** *Tokushima J. Exper. Med.* 1960, Aug., v. 7, No. 2, 124–32, 1 fig. [12 refs.]

This article, in English, adds to previous reports of studies made in small manganese mines [this *Bulletin*, 1960, v. 35, 113]. No ventilating facilities were found and dust counts remained high after crushing and blasting. Sources of drinking water contained 0·032–0·19 mgm. Mn per litre. Japanese handwriting illustrates micrographia and clumsy, abnormal arrangements. Symptoms and signs found among the 237 men and 91 women examined are listed in order of frequency. The women mostly dressed the ore, the men had various duties as miners. Extrapyramidal system disturbances, characteristic of Mn poisoning, developed within 6–24 months in those affected, with tremor an early sign, and they were more frequent in the younger subjects and in men exposed longer than 10 years. Chest X-rays were normal except 3 with silicotic shadows. The only abnormality in blood counts was a decreased red cell count; in animal experiments there had been gradual leucopenia. Hepatic disturbances were indicated by serum cobalt and Takada reactions and the presence of urobilinogen.

Another table shows group measurements for the patellar reflex threshold, strength of back muscles, vital capacity and length of breath holding, to be less, and muscular incoordination to be greater, in Group A who had neurological signs than in Group B who had none, except the vital capacity value in the women. The blood Mn content in 12 Group A men ranged from 3 to 82 μgm. per decilitre and the urine from 0 to 90 μgm. per litre. Basal metabolism was accelerated 10%—68·88% in 14 of 16 miners tested. None had hypertension. Density of hair in 31 exposed workers was greater than in 22 non-exposed. Among the 31 it was greater in those with no muscle or nervous system affections than in those with these signs of poisoning. A similar tendency has been described in the Mn content of hair. This suggests a relationship between the ability to excrete Mn and the development of poisoning.
M. Patricia Fitzsimons

TSUZUKI, A. **[An Experimental Study on Chromium Poisoning especially on the Chromium Content in the Poisoned Organs as estimated by Polarography]** *Igaku Kenkyu.* Fukuoka. 1959, May, v. 29, No. 5, 1578–97, 5 charts. [27 refs.] [In Japanese.] English summary.

Tissue concentrations in rats acutely poisoned by injection of chromium trioxide varied. When much chromium was retained, comparatively little was found in liver, kidney and intestine, a large amount in brain and, in only 1 case, in lung. Skin erosions, nasal and intramuscular bleeding and congestion and hypertrophy of liver, spleen and heart were noted. Rats chronically poisoned by 1 c.c. of 0·5% solution per kgm. injected on alternate days were killed after 1, 2 or 3 months. Elimination in liver, intestine, skin and fur increased for 2 months, and at first kidney excretion was normal. In brain and lungs the amount gradually decreased. In the heart it decreased and later increased. Little was found in muscle. No methaemoglobin was found after daily injections for 1 week, nor after potassium bichromate injections. Deductions are made of possible effects on chromaphil tissue, though, in the English summary, no supporting details are given. *M. Patricia Fitzsimons*

YANO, H. **[An Experimental Study on the Cobalt Poisoning in Rats and Polarographic Determination of Cobalt Contents in the Tissues and Organs]** *Igaku Kenkyu.* Fukuoka. 1959, Mar., v. 29, No. 3, 769–91, 6 charts & 8 figs. [30 refs.] [In Japanese.] English summary 792–4.

For acute poisoning 5% or 3% solutions of cobaltous chloride were injected subcutaneously, and for chronic

poisoning 0·5% or 1% solutions for periods up to 3 months, some rats being given 0·5 ml. of the 0·5% solution per kgm. each day. Some were observed for 5 months. Serial blood samples for 1 month after 1% solutions showed marked increase in haemoglobin on the 8th day and then a steady increase to constant levels.

Deaths from acute poisoning took place within 1 month. (Fatal shock had followed 10% solutions.) Epistaxis, epilation, haemorrhagic or necrotic skin ulceration, diarrhoea, haematemesis, lethargy and anorexia were noted. Hypertrophy of the spleen was probably due to hyperaemia. The metal was found in all organs, the most in hair, least in brain, lungs and skin and significant amounts in liver and intestine. Control animals showed traces in lung, brain, heart and hair and 46 gamma % in liver.

Chronic poisoning produced few toxic signs and no bleeding. After 1 month the metal distribution in descending order was hair, liver, kidney, large intestine, lung, heart, pancreas, small intestine, skin, muscle and brain, the differences being small. Survivors 2 months after had increased amounts, especially in liver, kidney, muscle and intestine. After injections for 3 months, liver and kidney contained less though their weights had increased, and the hair contained more, suggesting liver, kidney and skin excretion. However, other organs contained more than after injections for 2 months, except the brain where the amounts were always small, regardless of dose. Steady excretion took place through the large intestine after administration ceased. There were no marked nervous system disturbances.

M. Patricia Fitzsimons

STEINBERG, H. J. **Accidental Thallium Poisoning in Adults.** *Southern Med. J.* 1961, Jan., v. 54, No. 1, 6–9. [12 refs.]

This paper contains a short review of some of the literature of thallium poisoning. In recent years, apart from industrial poisoning, the emphasis has been upon the recognition of the poisoning in children who have ingested thallium contained in rodenticides and insecticides. There are, however, occasional reports of cases of accidental thallium poisoning in adults in which the source of the poison could not be ascertained.

4 cases of adult thallium poisoning (with mention of 3 other cases) are described here and in these it could only be assumed that the food consumed may have been contaminated by pesticides.

Particular emphasis is placed on the psychiatric manifestations of thallium poisoning reported also by other observers and which were present in 2 of the present cases. Unless one is aware of such manifestations in cases of thallium poisoning these might easily be misdiagnosed as disorders of personality or as neuroses.

The most striking of the cases described was in a 36-year-old woman of the U.S. Women's Army Corps who had an excellent record in her 12 years of active duty and had recently been promoted. In a few months her work began steadily to deteriorate, she became very forgetful and her personal appearance was untidy and dirty. On examination, psychological tests revealed definite evidence of brain damage. Her clinical state is described at length and it was found that there was a urinary excretion of thallium of 1·06 mgm. in 24 hours. She improved so much under medical care that she was discharged back to duty although she still showed occasionally some residual evidence of her illness.

In all 4 of these patients, one of whom was symptomless but had organic brain damage revealed by tests, thallium was being excreted in the urine.

It is again stressed in the summary that in thallium poisoning in addition to anorexia, fatigue, pain in the limbs, neuritis, incoordination, loss of hair, dry skin and visual disturbances there may be organic brain damage which is slow to recover and may be permanent.

[See this *Bulletin*, 1934, v. 9, 752; 1959, v. 34, 459.]

M. E. Delafield

CASARETT, L. J., BLESS, S., KATZ, R. & SCOTT, J. K. **Retention and Fate of Iridium-192 in Rats following Inhalation.** *Amer. Indust. Hyg. Ass. J.* 1960, Oct., v. 21, No. 5, 414–18, 7 figs.

30 female rats (Rochester colony; mean weight about 150 gm.) were exposed to an iridium-192 aerosol in groups of 6 rats. The mean air concentration was 1·15 micro-curies per litre (range 1·09–1·18) or about $1{\cdot}2410^{-4}$ μgm. per litre. Air samples were taken with type AA membrane filters (Millipore) with a sampling rate of 100 cc. per minute. After an exposure of about 30 minutes, the rats were removed and either killed immediately or put into metabolism cages for later autopsy. Pairs of rats were killed at 3 hours and at 1, 3, 6, 9, 13 and 14 days after exposure in addition to those killed immediately upon termination of the exposure. Major organs and tissues were counted in a Texaco Well Counter with an efficiency of about 2·5%. Tissue sections were taken for pathological examination and for auto-radiography.

The total material deposited in the rats varied from 0·35 micro-curies to 5·1 micro-curies with a mean value of 2·6 micro-curies. By calculating the total dose as a percentage of the total iridium "available" for deposition, an estimated mean deposition value of about 58% was obtained, although the entire range of deposition was from 10 to 95%. It appears that of the material deposited in the rats, more than 95% of the dose was deposited in the upper respiratory tract. Essentially the entire dose of iridium was cleared from the body by the end of the experimental period (14 days). The clearance occurred chiefly *via* the gastrointestinal tract which contained an average of 46% of the dose 3 hours after exposure, about 18% at 24 hours, in addition to that found in the faeces at that time, and less than 1% of the dose 3 days after exposure. No significant changes were found on pathological examination of the tissues.

The aerosol count median diameter was 0·07 μ with a geometric standard deviation of 1·5 (mass median diameter of about 0·12 μ). The authors were surprised at the large upper respiratory deposition in view of the particle size distribution found in this experiment and they suggest that a solution to this enigma might be found in a more careful examination of the physical chemical properties of the iridium suspension. They are also of the opinion that iridium particles, if properly

sized, would be useful in the study of lung clearance mechanisms.

It would appear, from this study, that in terms of either the chemical or radiation dose, the most vulnerable tissue after inhalation is the gastrointestinal tract, followed by the respiratory tract, and other tissues are subject to insignificant doses by comparison.

P. J. R. Challen

McLean, J. A. **Blood Dyscrasia after Contact with Petrol containing Benzol.** *Med. J. Australia.* 1960, Nov. 26, v. 2, No. 22, 845–9, 1 graph. [12 refs.]

A diversity of blood disorders is shown by a haematologist to follow the use of petrols containing benzol (benzene). Fatal aplastic anaemia occurred in 3 patients as follows: a boy aged 14 who syphoned petrol by mouth, for a boat, 3 times a week for 8 weeks, died 2 months later with terminal staphylococcal pneumonia; a garage hand aged 18, employed for 4 months, who aspirated petrol when occasionally syphoning, died in 3 months of cerebral haemorrhage; a deaf man who became a petrol-pump attendant at the age of 65 became ill after 6 months, having inhaled high concentrations when putting his ear near the opening to judge filling, and died 9 months later. A man aged 37, who in 1958 aspirated a large quantity of petrol while attempting to unblock a motor-car pipe, developed aspiration pneumonia and chronic neutropenia, shown in 1959 not to be due to sulphadimidine administered earlier. A motor mechanic aged 34 who for 2 years washed car parts with petrol which he occasionally syphoned by mouth had thrombocytopenic purpura. These petrols contained 10% benzol.

Haemolytic anaemia, with cellular proliferation of the marrow, myelofibrosis and splenomegaly developed in an oil company employee aged 27 after 12 months' exposure to petrol vapour in an enclosed yard. This petrol contained not more than 1% benzol. In 1955, 5 months after the onset, when the haematocrit fell from 34% to 27% and there was a raised indirect serum bilirubin, the red cell life was one-half of normal. When on cortisone, with the haematocrit steady at 38%, other isotope investigations show a red cell survival of 25% normal with a compensatory active haemopoiesis and early destruction of tagged cells by the spleen. No abnormality was found by the Heinz body incubation test. The glutathione stability test and, later, liver function tests and serum protein electrophoretic patterns were normal. Immature myeloid cells and normoblasts have increased in the blood but there is no evidence of leukaemia.

M. Patricia Fitzsimons

Lachnit, V. & Pietschmann, H. Leberschädigungen bei akuter beruflicher Tetrachlorkohlenstoffvergiftung. **[Liver Damage in Acute Occupational Carbon Tetrachloride Poisoning]** *Arch. f. Gewerbepath. u. Gewerbehyg.* 1960, v. 18, No. 3, 337–42, 1 fig. [27 refs.]

Carbon tetrachloride is still used occasionally in industry as a solvent in spite of its being so toxic a chemical. The literature quoted here contains reports on its toxic effects not only on the liver but also on the reticulo-endothelial system and as causing aplastic anaemia [this *Bulletin*, 1954, v. 29, 1073].

This paper contains a full account with clinical details and the results of laboratory investigation of 2 cases of carbon tetrachloride poisoning in 2 men who had been exposed for a few hours to the chemical which they had been using for cleaning machine parts.

Although the symptoms and signs of poisoning were not extremely severe, proof of intense liver damage was obtained by the high values of activity determined in the serum glutaminic-acid-oxalacetic acid transaminase and the serum aldolase tests. Biopsy samples of liver tissue showed extensive degenerative changes including some necrosis.

M. E. Delafield

Finzel, M. Leber- und Nierenschäden nach einmaliger Einwirkung von Tetrachlorkohlenstoff. **[Liver and Kidney Damage from a Single Exposure to Carbon Tetrachloride]** *Zent. f. Arbeitsmed. u. Arbeitsschutz.* 1960, Oct., v. 10, No. 10, 235–8.

The 3 cases of carbon tetrachloride poisoning described in this paper resulted from the inhalation of carbon tetrachloride during a single work shift. They are published because the opinion that kidney and liver damage due to the poison only follows long continuing exposure is still frequently expressed.

The cases were in 3 women workers, 2 of whom were employed in making toys and the other in cleaning textiles. Because of a shortage of the chemicals usually employed in their work carbon tetrachloride was used instead. Within a short time of beginning work with carbon tetrachloride the women were taken ill with giddiness, nausea and vomiting. There are full hospital case reports with clinical and laboratory findings.

The narcotic effects of the inhalation of carbon tetrachloride were relatively moderate but there was some evidence of severe hepatic and renal damage which necessitated a stay in hospital for several months. Although the 3 women were greatly improved the damage sustained has not healed fully.

The points made in the conclusions are that the existing legal control of the sale and use of carbon tetrachloride is inadequate and that it is nowadays unnecessary to use this poisonous substance for cleaning purposes or for fire-fighting.

M. E. Delafield

Wirtschafter, Z. T. & Tsujimura, J. K. **Serum Glutamic Oxalacetic Transaminase. Specificity of Values in Hepatocellular Injury.** *Arch. Environment. Health.* Chicago. 1961, Jan., v. 2, No. 1, 16–22, 5 figs.

"An attempt to correlate SGO-T values with the histological liver sections in 20 normal rats, and in 48 rats exposed to a single injection of carbon tetrachloride failed in 7 of the 48 experimental animals.

"High SGO-T values can be correlated with marked hepatocellular damage.

"Low or normal SGO-T values cannot be used to exclude the presence of significant hepatic necrosis."

BARTONÍCEK, V. Der Einfluss einiger Stoffe auf die Harnausscheidung von Trichloräthanol und Trichloressigsäure beim Kaninchen. [**The Influence of Certain Compounds on the Urinary Excretion of Trichloroethanol and Trichloroacetic Acid in Rabbits**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1960, v. 18, No. 3, 317–26, 2 figs. [19 refs.]

It has been shown in a previous paper by the author and SOUCEK that trichloroethylene is oxidized and excreted by the rabbit chiefly as trichloroethanol and trichloroacetic acid [this *Bulletin*, 1959, v. 34, 1140]. The work described here with experimental details was carried out on 6 rabbits in order to study the effect of glucose, fructose and lactic acid on the excretion of the oxidation products of trichloroethylene. The reasons for these experiments were the observations recorded in the literature that glucose, fructose and lactic acid accelerate the disappearance of ethanol from the blood and it was thought that a similar acceleration might occur with trichloroethanol. In some further experiments ethanol was also tested for a possible effect on the excretion of the oxidation products of trichloroethylene since chronic alcoholics are known to have an intolerance to trichloroethylene.

The 6 rabbits were given trichloroethylene (1·0 ml.) by intramuscular injection 3 times a week for 7 weeks before the influence of intravenous glucose and the other substances was tested.

The main results of these experiments on only 6 rabbits were that none of the substances (glucose, etc.) had any influence on the amount of trichloroacetic acid excreted. The amount of trichloroethanol excreted was increased by glucose (13%) and ethanol (9%) but diminished by sodium lactate (7%) and fructose (12%). Although the observations are so few in number the assumption is made that lactate and fructose given repeatedly by intravenous injection might have a protective effect on workers chronically exposed to trichloroethylene. *M. E. Delafield*

BERGHOUT, C. F. **Spray Painting without Compressed Air.** *Arch. Environment. Health.* Chicago. 1960, Dec., v. 1, No. 6, 534–9, 3 figs.

Hydraulic pressure spray guns of 2 types were tested for health, safety and fire hazards. From the number of breathing zone air samples analyzed for Pb, chromate or solvent, certain general conclusions were drawn though more are required for valid comparisons. The objective was to determine whether an air velocity of less than 150 feet per minute (f.p.m.) would be safe for ventilation control of spray booths with 2 methods of delivering paint, by means of high pressure or heat-with-pressure equipment. Vehicles and missile containers were sprayed in a modified down-draught vehicle booth, and vehicle parts in a smaller open-face booth, at air velocities of 62, 105 or 130 f.p.m. Analyses are given of primer, thinner and enamels.

Chromate was only tested at 62 f.p.m. with the heat-with-pressure method and was much higher than the MAC. With both methods Pb concentrations were above the MAC, except in 1 instance of using heat-with-pressure at 105 f.p.m. when adequate air-flow was probably helped by the nature of the truck being painted.

Dangerous concentrations of explosive vapour were recorded in the vehicle booth with velocities below 100–110 f.p.m., and a fire hazard was observed from accumulated overspray residue. For missile container spraying a ventilating rate of at least 150 f.p.m. was necessary in the vehicle booth and, for health protection, in the open-face booth. In the latter handling or turning devices would be necessary, and it was questionable whether alarm systems could be adapted to the heat-with-pressure method or low air velocities.

Tests were also carried out by both methods for vehicle spraying in an open shop with good general ventilation. This was dangerous from every standpoint, and here the concentrations of solvent also were above the MAC. *M. Patricia Fitzsimons.*

ZORN, O. & KRUGER, P. D. **The Problem of Chronic Carbon Monoxide Poisoning.** *Indust. Med. & Surgery.* Miami. 1960, Dec., v. 29, No. 12, 580–81.

"The only way to resolve the problem"—the uncertainty of the existence of chronic poisoning—"would be through parallel studies of workers exposed to carbon monoxide and a non-exposed control group with a statistical examination of the results." A study was carried out in coke and metallurgical works on 868 lightly exposed workers, 140 with greater exposure and 306 non-exposed controls. This English translation of the account presented at the recent international congress of occupational health in Now York gives the data of symptoms only. There were no significant differences between controls and those lightly exposed. Such findings as polycythaemia, anaemia, blood pressure changes, circulatory changes and neurological deficiences were divided evenly among these groups.

Among the heavily exposed, mostly blast furnace and generator operators, there was a significant increase in the classical, though unspecific trio of headache, dizziness and weakness, but this occurred at work, disappeared afterwards and was not present during holidays. The picture was that of light, repeated acute CO poisoning without after-effects.

Additional conclusions were drawn. Levels of CO such as are found in streets, commonly have no clinical effect. The possibility of developing hypersensitivity is unlikely. Tolerance differs and is related to the state of health of the individual. The theory that repeated exposures produced an increasingly stronger effect was not proved. Tolerance may be overstepped by prolonged exposure to low concentrations which may lead to slowly developing acute poisoning. There were no medical grounds for the concept of chronic CO poisoning but instead "light recurring carbon monoxide poisoning."

M. Patricia Fitzsimons

BIELECKA, Wiesława, BAHYRYCZ-LUDERA, Maria & SPETT, K. Działanie cytochromu C na poziom kwasów metabolicznych w ostrym zatruciu co u świnek morskich. [**Effect of Cytochrome C on the Level of Metabolic Acids in the Acute Carbon Monoxide Poisoning of Guineapigs.**] *Med. Pracy.* 1960, v. 11, No. 5, 311–14.

The English summary appended to the paper is as follows:—

"In order to explain the factors causing acidosis following carbon monoxide poisoning, the level of acetone bodies, alphaketo-acids and lactic acid in blood of guinea-pigs was investigated. It was stated that the content of acetone bodies was not increased, however the concentrations of alpha-keto-acids and of lactic acid was significantly higher. On the basis of determined amounts of lactic acid in blood it was stated that 50 p.c. of acidosis in the case of carbon monoxide acute poisoning is provoked by the lactic acid. The alpha-keto-acids play no part in this phenomenon.

"The intravenous injection of about 6·25 mg/kg of body weight of cytochrome c, made before poisoning prevents very effectively the increase of lactic acid, and has no influence on the level of alpha-keto-acids."

LANG, J. & STINTZY, F. Un cas d'intoxication lente à l'acide cyanhydrique par l'acétone-cyanhydrine. [**A Case of Delayed Hydrocyanic Acid Poisoning from Acetone-cyanhydrin**] *Arch. Malad. Professionnelles.* Paris. 1960, Oct.–Nov., v. 21, Nos. 10/11, 652–7.

This is a clinical description of a young man who recovered from convulsive coma treated symptomatically since the aetiology remained obscure until renewed questioning. Unknown to his companions doing similar work, and unaffected, he had before noon dismantled and flushed a pipe which contained perhaps 30–40 ml. acetone cyanhydrin (AC). The washings soaked into his clothing. AC decomposes into acetone and HCN in an alkaline medium. Such would be the sweat on an alcoholic's skin exerting himself in a hot workroom. The acetone would facilitate absorption. Some 5 hours later he had a headache, nausea, weakness and giddiness, but finished work and changed his clothes. At home, he vomited some bile and went to bed at 6.45 p.m., his parents ignoring the staggering gait because of his alcoholic habits.

Shortly afterwards his mother found him unconscious, rigid with the back arched, blue and frothing at mouth and nostrils. He arrived at hospital in deep coma, flaccid, cyanosed, with stertorous, slow, regular breathing, good pulse, low blood pressure, dilated, fixed pupils and diminished reflexes. Acetone smelt in the breath was not found in the urine. Chest X-ray and other examinations were negative. Profuse, repeated diuresis was confusing. For 3 hours from 9 p.m. violent clonic convulsions alternated with tonic convulsions and opisthotonos, culminating in a severe paroxysm and apnoea for 45 seconds, followed by flaccidity and sweating. Pupils, reflexes and blood pressure became normal. The patient responded slightly to auditory stimulus and slept for 6 hours. He awoke with amnesia since going to bed, and had pyrexia. Investigations, including blood sugar and urea, were normal. He had been treated with oxygen, probably life-saving, and a barbiturate, an analeptic and a circulatory stimulant, probably useless to say the least. After waking, he was transfused with physiological serum containing Mg glutamate and vitamin B1, which probably helped. Methods of treating HCN poisoning are described and evaluated. *M. Patricia Fitzsimons*

BILLEWICZ-STANKIEWICZ, J. & PAWŁOWSKI, L. Badania doświadczalne nad wpływem wdychania azotniaku na wyższą czynnośc nerwową zwierząt. [**Experimental Studies on the Effect of Calcium Cyanamide Inhalation upon the Higher Nervous Activity of Animals**] *Med. Pracy.* 1960, v. 11, No. 6, 433–40, 2 figs.

The English summary appended to the paper is as follows:—

"The investigations on the effect of inhalation of calcium cyanamide dust upon the higher nervous activity were carried out in rats. Conditional reflexes were created in rats. These reflexes were stereotypical for the following stimuli and ranged as follows: 1 and 2—bell sound, 3 and 4—red light, 5—bell sound, 6—tinkle roar (buffer differentiating stimulus), 7 and 8—bell sound, 9 and 10—red light. Resting in the inhalation chamber and the roar of the electric aspirator provoke in rats no real changes in the stereotype. Shorter exposures to the action of calcium cynamide dust suspension (2·9 mg/litre 1—2300 thousand particles in 1 litre of air) in the limits from 10 to 50 minutes have caused the weakening of the inhibitory processes. The longer inhalation of calcium cyanamide (1–2 hours) in all animals have led to the weakening and then to the disappearance of many positive reflex reactions. These phenomena lasted up to several hours after the end of inhalation. During the next period of eleven days after stopping the exposure to the calcium cyanamide action, the conditional reflexes came to the normal state. Dust suspension of a concentration smaller about by half (1·6 mg/litre—1300 thousand particles in 1 litre) did not cause changes in the conditional reflex activity of rats.

"The authors come to the conclusion, that the threshold concentration of dust suspension influencing the highest nervous activity of rats lays between 1300 thousand to 2300 thousand particles in 1 litre of air, whereas threshold activity time is ranging from several to ninety minutes."

NAU, C. A., NEAL, J. & STEMBRIDGE, V. A. **A Study of the Physiological Effects of Carbon Black. III. Adsorption and Elution Potentials; Subcutaneous Injections.** *Arch. Environment. Health.* Chicago. 1960, Dec., v. 1, No. 6, 512–33, 1 fig.

In addition to 10 long tables showing whether tumour formation after injection was found or not, others give nomenclature and properties of several carbon blacks. Carbon black is essentially carbon combined with hydrogen and oxygen resulting from the incomplete combustion of gas, oil and oil sludges. It is used as a colouring in rubber goods, inks and certain food products. Blacks, representative of all in common use, were used in this section of extensive studies begun in 1949 [this *Bulletin,* 1959, v. 34, 632].

The maximum amount of benzpyrene adsorbed on 100 mgm. channel black was 9μgm. This adsorbed component could not be extracted with benzene at room temperature. Tests with plasma and gastric juice showed that neither eluted any significant adsorbed component

from a channel or a furnace black suspended for 7 days. No significant extraction of these blacks was accomplished in 7 days by gastric juice with 10% cooking oil.

Different amounts of various preparations in water, cottonseed oil or tricaprylin were injected in many groups of mice, mainly subcutaneously, sometimes intraperitoneally. Some guineapigs and rabbits were used. All organs were examined microscopically. Mice were observed for 20 months. The following preparations were injected, positive results indicating tumour formation, negative, no tumours: channel or furnace blacks, negative; blacks from which benzene extractable components, when present, had been removed, negative; benzene extractives (those from furnace blacks when injected in oil), positive, others negative; blacks to which previously removed benzene extractives had been readsorbed, negative; cooking oil in which blacks were suspended for 1–6 months, positive; methylcholanthrene or benzpyrene, positive; these 2 carcinogens adsorbed on blacks, negative; tricaprylin or cooking oil, some positive.

M. Patricia Fitzsimons

Vigliani, E. C. & Parmeggiani, L. Analogie e differenze fra le dosi massime ammissibili nel rischio radiologico e le massime concentrazioni tollerabili negli altri rischi lavorativi convenzionali. [**Analogies and Differences in Maximum Permissible Doses in Exposures to Radiological Radiation and other Conventional Working Risks**] *Med. d. Lavoro.* 1960, Nov., v. 51, No. 11, 678–88. English summary.

Ionizing radiations may cause genetic changes of the utmost importance; they have a cumulative effect which may produce leukaemia and may shorten life; repeated small doses may lead to serious lesions, perhaps after a "silent period" through delayed action, and there are often no warning signs and symptoms in time for effective preventive measures to be taken before permanent injury has been sustained. No sort of immunity, acquired or congenital, is known against radiation.

By contrast, industrial poisons have little or no genetic action; they are quite safe up to certain defined doses, even when these are repeated many times; some have a cumulative, perhaps delayed, toxicity which is manifested by timely signs and symptoms which allow of preventive steps effectively being taken. The toxic chemicals which may be absorbed through the hazards of industrial or other employment give rise to allergic conditions and may produce reactions which can be utilized as diagnostic help.

The injurious action of ionizing radiations follows a more or less constant pattern, but the consequences of different industrial poisons vary widely. Radioactivity can be more exactly controlled than can the risks from the use of toxic substances in industry or other work; though many of the latter kinds of hazard have been known for a much longer time, the protection of workers against radiological risks has, in fact, made the better progress. The work of the various international agencies concerned should help to achieve agreement and provide a uniform code of maximum permissible doses in exposure to ionizing radiations and a standard schedule of tolerance limits of concentration for those toxic substances which are known to involve occupational risks.

J. Cauchi

Food and Nutrition

The order in this section is:—**General; Foodstuffs; Food Poisoning.**

GENERAL

Abramson, J. H., Slome, C. & Ward, Nancy T. **Diet and Health of a Group of African Agricultural Workers in South Africa.** *Amer. J. Clin. Nutrition.* 1960, Nov.–Dec., v. 8, No. 6, 875–84. [31 refs.]

The report deals with a survey of the diet and health of 118 African agricultural workers. Most of the men were Pondo or Zulu who had been recruited from rural areas to work for 6 months on a contract basis. They were housed in barracks at their place of work. Food intakes were found to approximate closely to the official ration scale, with little waste of food or consumption of extra foods. The ration supplied 4,876 calories and 142·6 gm. of protein daily; but animal protein was only 24·2 gm., and vitamin A, ascorbic acid, riboflavin and calcium intakes were much below recommended amounts. The diet was based largely on maize (76% of the total calories) and contained only small quantities of meat and vegetables. Meals were bulky and monotonous, and food hygiene was poor.

Some signs of nutritional deficiency were found in all the men: 99% showed tongue changes, skin changes were seen in 88% and abnormalities of the gums and lips in 70%. Severe deficiency signs or other illnesses were rare. On the whole the men were thin for their heights, when compared with urban Zulus. They tended to put on weight during their first 2 months of work, and to lose weight subsequently, probably because the monotony of the meals became progressively less tolerable. The employers claimed that the morale of

the men was poor and their productivity low; this was confirmed during the investigation. Much of the discontent was caused by the quality of the food and the manner in which it was served. However, there appeared to be no correlation of nutritional status with productivity, and only limited correlation between morale and nutritional status. The authors concluded that the men were somewhat malnourished and suggested modifications of their diet on the basis of the FAO recommendations for maize diets, but they pointed out that the unsatisfactory diet was only a part of generally poor and unhygienic living conditions.

R. Schwartz

FOODSTUFFS

Composition and Bacteriological Control

McCance, R. A. & Widdowson, E. M. **The Composition of Foods.** *Med. Res. Council Spec. Rep. Ser. No. 297* (3rd revised edition of *Spec. Rep. No. 235*). pp. viii + 252. [Numerous refs.] 1960. London: H.M. Stationery Office. [30s.]

Over the past 20 years, "McCance and Widdowson" has been an essential manual for those concerned in Great Britain with the dietary treatment of disease, or with dietary and nutritional studies. The last edition, published in 1946 [this *Bulletin*, 1946, v. 21, 476], contained information about a number of foods that were in general use during the period of wartime and post-war rationing. Since then, many new proprietary foods have come into general use, and there have been changes in the ingredients of common foods.

This new, third-revised edition is divided into 3 parts. Part I—Calorific Constituents, Water, and Minerals, by R. A. McCance, E. M. Widdowson, and D. A. T. Southgate, is a revision and expansion of the tables given in previous editions, containing analyses for water, nitrogen, fat, carbohydrates, minerals, and calorie-value of 663 different foods and cooked dishes, including about 100 new analyses of foods not previously recorded. All analyses of proprietary foods have been checked with the manufacturers. Where there has been a change of formula, new analyses have been made, and the section on the chemical composition of cooked dishes has been revised. There are many new analyses of alcoholic beverages and sweets. As in the earlier editions, two sets of tables express the quantities of nutrients per 100 gm. and per ounce.

Part II and Part III are new. Part II—Vitamins, by I. M. Barrett and E. M. Widdowson—gives the amounts per 100 gm. in many of the foods included in Part I, of vitamin A, carotene, vitamin D, thiamine, riboflavine, nicotinic acid and ascorbic acid, and in a smaller number of foods, of pantothenic acid, vitamin B6, biotin, folic acid, vitamin B12, and total tocopherols. These tables have been prepared from a survey of published results. About a thousand publications were consulted, and 970 references, on which the selected values were based, are listed.

Part III—Amino-Acids, by B. P. Hughes—gives amino-acid contents, per gm. of nitrogen, of foods in five categories—cereals, milk products, eggs, meat and fish, nuts, and vegetables. Values for two groups of amino-acids are given; one group contains the ten "essential" amino-acids, together with cystine and tyrosine; the second group contains alanine, glycine, proline, serine, aspartic acid and glutamic acid. The values, like those given for vitamins, have been obtained from a survey of published reports of analyses. The expression of amino-acid values in terms of total nitrogen-content of a relatively few broader categories of food, permits the use of simplified and condensed tables, for the nitrogen content of particular foods is given in Part I.

The revised expansion contained in Part I has been found by experience in a field dietary survey to give an even more comprehensive list of foods, including cooked dishes, preserves and sauces, used in Great Britain, than the former edition. A number of values, such as those for bread, confectionery and sweetmeats, influenced as they were by wartime shortages, had to be taken with reservations, but are now reliable. The utility and value of the book are greatly increased by the addition of the new sections on vitamins and amino-acids. From the data given it is possible to qualify the crude figures for protein based on total nitrogen content given in Part I, by reference to the pattern of amino-acids given in Part III, and to arrive at a protein score by comparison with a hypothetical ideal reference protein. These additions allow for a much more comprehensively based assessment of dietary values. *T. P. Eddy*

Burr, H. K. & Elliott, R. P. **Quality and Safety in Frozen Foods [Report to the Council on Foods and Nutrition** (White, P. L., Secretary).] *J. Amer. Med. Ass.* 1960, Oct. 29, v. 174, No. 9, 1178–80, 1 fig. [20 refs.]

The annual consumption of frozen foods in the U.S.A. is now nearly 30 lb. per head; they are described as safe and nutritious and said to have good flavour. Defects from improper or prolonged frozen storage are primarily chemical or physical; bacterial spoilage occurs only after gross mishandling.

Food-poisoning organisms may be present on raw frozen foods but they will not increase unless the refrigeration is inadequate. *Trichinella spiralis* dies out rapidly in frozen pork.

The Association of Food and Drug Officials of the United States is developing a frozen-food handling code which will require frozen foods to be held at 0°F. or

below, with only brief excursions to higher temperatures until sold to the consumer. Processors, transportation companies, distributors and retailers are collaborating in the development of voluntary standards for industrial practice. Microbiological standards are not yet included, although some firms have set their own limits, and official standards have been incorporated into specifications of the Quartermaster Corps and regulations of New York City and Massachusetts. *Betty C. Hobbs*

FLIPPIN, R. S.; MICKELSON, M. N. **Use of Salmonellae Antagonists in fermenting Egg White. I. Microbial Antagonists of Salmonellae** [FLIPPIN & MICKELSON]. *Applied Microbiol.* Baltimore. 1960, Nov., v. 8, No. 6, 366–70. [19 refs.] **II. Microbiological Methods for the Elimination of Salmonellae from Egg White** [MICKELSON & FLIPPIN]. *Ibid.*, 371–7, 1 fig. [16 refs.]

I. With 3 salmonella cultures, Salm. Senftenberg (2623), Salm. Oranienburg (200E) and *Salm. typhimurium* (TM-1) inhibitory screening tests were carried out on 700 strains of streptomyces, yeasts, bacteria and fungi isolated from soil, water, fruit, bovine rumen contents and stools from chicks, dogs, cats, mice, cattle and human beings. 25 cultures showed activity against one or more of the salmonellae. *Bacillus polymyxa* showed the greatest zones of inhibition to all 3 salmonellae; but the organism would not grow in egg white even when supplemented by other substances. Gram-positive organisms were inhibited by lysozyme and other antibacterial protein in egg white whereas Gram-negative bacteria grew well. 17 of the antagonistic cultures were unsatisfactory because they liquefied gelatin, others also showed proteolytic activity. *Escherichia coli* fermented glucose and 4 strains were antagonistic and appeared to have no undesirable effect on egg white.

The presence of 0·25–1·0% glucose in nutrient broth together with the antagonistic *E. coli* (6–204–55) eliminated Salm. Senftenberg 2623 in 72 hours.

II. The use of a non-pathogenic strain of *Escherichia coli* (6–204–55) for the elimination of glucose and salmonellae (Senftenberg, Oranienburg, and *typhi-murium*) from liquid egg white was further investigated. In nutrient broth with added glucose Salm. Senftenberg did not survive in the presence of *E. coli*. In egg white media complete destruction of Salm. Senftenberg was obtained only after the addition of 0·5% H_2O_2 following a 48-hour fermentation period with *E. coli*.

The numbers of *E. coli* present seemed of little significance in the inhibition of salmonellae. Difco nutrient broth and agar, Difco tryptone glucose extract broth and agar, and brilliant green selenite broth agar [STOKES and OSBORNE, *Applied Microbiol.*, Baltimore, 1955, v. 3, 217; this *Bulletin*, 1956, v. 31, (444)] were used for the work. *Betty C. Hobbs*

SHAPIRO, Jennie E. & HOLDER, I. A. **Effect of Antibiotic and Chemical Dips on the Microflora of Packaged Salad Mix.** *Applied Microbiol.* Baltimore. 1960, Nov., v. 8, No. 6, 341–5.

Salad greens containing a mixture of celery, chicory, escarole, cabbage (red and white), red radish, celery cabbage, parsley and carrot, packed in ventilated plastic bags and obtained from local vendors and a processing plant were examined bacteriologically. Counts on nutrient agar varied from 11–170 million per gm. of spun-dried vegetable; samples obtained at the packaging plant gave counts which were significantly lower than those from samples taken at the time of delivery to the retailer; organisms of the *Pseudomonas* and *Bacterium* groups predominated. The samples were divided, one portion rinsed in tap water (control) and the other treated. On the basis of the sensitivity of the organisms oxytetracycline (50 p.p.m.), Biostat (50 p.p.m. oxytetracycline) and citric acid (150 and 500 p.p.m.) all buffered at *p*H 5·0 and also tartaric acid (500–1500 p.p.m.) were used as dipping solutions. Samples were dipped, shaken in a vegetable basket to remove excess moisture, repacked, stored at 10°C. and cultured on successive days for 1 week. Oxytetracycline and Biostat were effective in decreasing the microbial population and maintained low counts for a week. Citric acid and tartaric acid were effective in lowering counts, but inhibitory action was not so prolonged as that of the antibiotics.

Betty C. Hobbs

WINKLE, S. & ADAM, W. Über die Dampfdesinfektion von Fischmehl. [**The Steam Disinfection of Fish Meal**] *Desinfektion u. Gesundheitswesen.* 1960, July–Aug., v. 52, Nos. 7/8, 97–101, 1 fig. [21 refs.]

Since 1953 there has occurred a large increase in Salmonella infections in Germany and the introduction of types of organisms, previously not met with in Germany, by the importation of foodstuffs. In this paper there is a description of the special danger from the importation of fish meal to be used for animal feeding. Fish meal has been imported into Germany for many years, before the second world war almost entirely from Norway and Japan when it was heat-treated and did not give rise to infection in animals. After the Korean war, however, increasing demand led to the importation of fish meal from under-developed countries such as Angola where the fish is dried under extremely unhygienic conditions. Bacteriological examination has shown that this fish meal is very heavily polluted with salmonellae of many different types [this *Bulletin*, 1956, v. 31, 1075, 1150]. It is therefore necessary to disinfect it and there is here described, with a diagram, a steam disinfector which has proved to be very effective at a temperature of about 100°C. maintained for from 4 to 35 minutes. The bacteriological techniques used for control of the efficacy of the apparatus are described. Salmonellae are definitely destroyed although thermo-resistant aerobic sporing organisms remained alive. *M. E. Delafield*

FOOD POISONING

PUBLIC HEALTH LAB. SERVICE. **Food Poisoning in England and Wales, 1959. A Report.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1960, Dec., v. 19, 224–37. [15 refs.]

7,846 incidents of food poisoning including general (295) and family (666) outbreaks and sporadic cases (6,885) were reported during 1959—7% more than in 1958 and 11% more than in 1957. There were 27 fatal cases, 15 due to *Salm. typhi-murium*, 2 to Salm. Newport, one each to *Salm. cholerae suis* var. *kunzendorf*, *Salm. enteritidis*, Salm. Thompson, Salm. Chester, Salm. Muenchen and Salm. Saint-Paul, one to *Staph. aureus* and three to *Cl. welchii*. 61% of incidents were due to *Salm. typhi-murium*, 35% to other salmonellae, 2% to staphylococci and 2% to *Cl. welchii*. Except for a small outbreak of solanine poisoning associated with potatoes cooked in their skins [WILSON, this *Bulletin*, 1960, v. 35, 447] no chemical food poisoning was reported. The cause was not discovered in 33% of incidents. The highest incidence occurred as usual during July, August and September.

Meatstuffs, associated with 143 of the 192 food vehicles given, are classified according to causal agents. As in previous years cold meats and made-up meatstuffs were largely responsible for staphylococcal outbreaks, and pre-cooked meats and meat dishes eaten either reheated or cold for *Cl. welchii* food poisoning; unfortunately few salmonella incidents were traced to specific foods.

4 outbreaks were associated with milk and one with cream (2 due to *Salm. typhi-murium* and 3 to *Staph. aureus*). In one large outbreak with 400 cases and 2 symptomless excretors, custards, trifles and cream confectionery were contaminated with a variety of different salmonellae, the source being egg albumen of American origin and also English frozen whole egg.

The proportion of incidents due to *Salm. typhi-murium* has fallen from 85% in 1954 to 63% in 1959 although the number has not altered; but the number of incidents due to other salmonellae has increased more than 3-fold and the proportion from 15% to 37%.

" Other " salmonellae are divided into endogenous and exogenous types and whereas the incidents due to endogenous types have increased irregularly those due to exogenous types have increased regularly from year to year. The more important increases include Salm. Newport incidents from 35 in 1954 to 319 in 1959, Salm. Thompson from 83 in 1954 to 207 in 1959, Salm. Heidelberg from 16 in 1954 to 308 in 1958 and 182 in 1959, *Salm. infantis* from 1 in 1954 to 57 in 1959 and Salm. Saint-Paul from 25 in 1954 to 95 in 1958 and 83 in 1959. Most of these salmonellae have been isolated repeatedly from egg products, meat, and meat products during the last few years, and now desiccated coconut can be added to the list of foodstuffs bringing salmonellae into the U.K. A table shows the types of salmonellae isolated from egg products, meats, and animal feeding stuffs and fertilizers in 1959 and indicates which strains commonly infect man. All but 6 of the 39 different types from eggs and egg products have been isolated from man in the last 5 years, likewise all of the 23 types isolated from meat and meat products in 1959. *Salm. typhi-murium* was the commonest salmonellae in both egg and meat products. Salm. Thompson is commonly isolated from human cases and egg products. Of the 63 types from animal feeding stuffs and fertilizers, 47 have been isolated from human cases.

Desiccated coconut is also contaminated with *Salm. paratyphi B* so that it joins Chinese egg products as a potential source not only of food poisoning but also of enteric fever. The heat-treatment of egg products is practicable, but the control of meat contamination is difficult and requires more combined work by veterinary and public health epidemiologists. [The treatment of desiccated coconut by heat, fumigation and irradiation is still being investigated.]

[For 1958 Report, see this *Bulletin*, 1960, v. 35, 240.]

Betty C. Hobbs

BISBINI, P., POSSATI, F. & MARINELLI, M. Due episodi di intossicazione alimentare da filetti di sgombro. **[Two Episodes of Food Poisoning Due to Mackerel Fillets]** *Nuovi Ann. d'Igiene e Microbiol.* 1960, Sept.–Oct., v. 11, No. 5, 377–86. [50 refs.] English summary (6 lines).

This is a report of 2 episodes of food poisoning which occurred after fillets of mackerel preserved in oil had been eaten. Each affected 2 persons.

(1) An elderly woman after having eaten mackerel fillets for her lunch was attacked 2 hours later by abdominal pain and diarrhoea. Her husband who ate some of the remaining fillets for his supper was also affected 2 hours later with headache, vomiting, violent diarrhoea, and fever and was admitted to hospital.

Samples of the mackerel fillets were bacteriologically examined both aerobically and anaerobically, but were negative except for a *Staphylococcus albus* which was shown to have no toxigenic properties. However, a Seitz filtrate when inoculated intracardially into guineapigs caused instant death, and death within a few hours when inoculated subcutaneously; when the filtrate was given to 10 guineapigs which had previously received an antihistaminic all were unaffected. Tests on the isolated guineapig intestine showed that 4–5 mgm. per gm. of histamine was present in the fillets.

(2) 3 clerks in the Bologna City Health Department ate rolls containing similar mackerel fillets preserved in oil; one was not affected, but about half an hour later the other 2 had congestion of the face and neck accompanied by a sense of heat, and headache, and after about 2 hours had vomiting and diarrhoea. Examination of fillets from the same tin gave both a *Staph. albus* and *Staph. citreus*, neither of which had any toxigenic properties. Intracardiac inoculation of a Seitz filtrate into guineapigs caused death within 5 minutes, and subcutaneous inoculation caused death within a few hours; tests on guineapigs treated previously with antihistaminics were negative, all were protected.

25 samples of mackerel, 15 of sardines, and 15 of tunny-fish, all preserved in oil, were then tested in a

similar manner, including Seitz filtrates, but no substances with a histamine-like action were detected.

The authors point out that in both episodes the fillets looked normal and no enterotoxic staphylococcus was found, while search for histamine-like substances in 55 other samples was negative.

They consider that the presence of histamine in considerable amounts points clearly to a considerable multiplication of bacteria since in fresh or in well preserved fish only traces of histamine are present. The contamination must have occurred before preservation since histamine is notably heat-stable. They consider that the estimation of this substance in addition to giving an idea of the freshness of the fish may also indicate the probable presence of substances not readily identifiable with the usual laboratory procedures. *W. K. Dunscombe*

Mycoses and Mycology

The order of diseases and fungi in this section is:—**General; Dermatophytes; Blastomyces; Histoplasma, Sporotrichum, Phialophora; Candida, Cryptococcus; Actinomyces, Nocardia; Aspergillus; Others.**

Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN.

GOODE, Patricia. **Vesicular Eruption associated with Griseofulvin.** [Correspondence.] *Lancet.* 1960, July 16, 155–6.

Most side effects of griseofulvin have so far been transient and mild but this is a record of a severe reaction in a woman treated for *Trichophyton rubrum* infection of the nails; the dose of griseofulvin was 1 gm. each day, divided into 4 doses. After the 20th day an irritating vesicular eruption appeared on hands and arms and in a few days there was gross swelling so that her hands could not be used, and the rash spread to the head and legs, in spite of treatment with prednisolone and chlorpheniramine maleate. The condition was so severe that griseofulvin was stopped; thereafter it cleared up. *Charles Wilcocks*

ENGLISH, Mary P.; GIBSON, Mary D.; DUNCAN, Ethel H. L. **Studies in the Epidemiology of Tinea Pedis. IV. Seeds and Soil** [ENGLISH, GIBSON & DUNCAN]. *Brit. Med. J.* 1960, Aug. 20, 573–6. [20 refs.] **V. Some Day Schools revisited** [ENGLISH & GIBSON]. *Ibid.*, 577–9.

IV. In pursuance of their studies on the epidemiology of tinea pedis in schools the authors compared the incidence of this infection in boys with that in girls. They found that this was higher in boys than in girls.

On analysis of their data, they found that greater use of out-of-school bathing facilities was made by boys than by girls, and that this applied also as regards the use of school showers. It was clear also from these data that boys wore a less ventilated type of footwear than girls.

When the incidence of infection in boys only was taken into account, although due note was taken of the influence of such factors as the use of showers (with or without wearing shoes), exchanging of footwear, and heavy sweating, no correlation between these factors and infection was observed. It was, however, indicated that the wearing of badly ventilated footwear was significant relative to the suitability of the "soil", and that, furthermore, one of the chief factors in bringing about infection in any group where the "soil" was favourable was the extent of contact with the inoculum.

As regards the observed difference in incidence of infection between boys and girls the authors were of the opinion that an overall factor, as yet undetermined, but which might be intrinsically linked with difference in sex, was probably operative in favour of girls being more resistant to infection than boys.

As it was possible that the incidence of infection in a given school could change after a period during which precautionary measures were observed and a greater awareness of possible infection prevailed, the authors decided to resurvey the incidence of infection in several schools previously visited.

V. Accordingly, approximately 2 years after previous visits had taken place, a survey was carried out along lines previously followed by the authors [see this *Bulletin*, 1957, v. 32, 574; 1959, v. 34, 1004; 1960, v. 35, 980].

Results showed little change in the overall incidence of tinea pedis or in the pattern of the species of dermatophyte causing it. However, when the incidence in 2 of the schools using the same swimming bath was compared it was found that 35% of the boys in one of these (with the lower incidence) had never made use of the baths in their poorly cleaned state as compared with only 17% of the boys in the other school (with the higher incidence). Furthermore, it was found that, in the first-mentioned school, "athlete's foot" had become a social stigma, whereas this was not so in the second school.

C. J. La Touche

NEVES, H. **Mycological Study of 519 Cases of Ringworm Infections in Portugal. Significance of Multiple Localizations. Tinea as a Single Infection.** *Mycopathologia.* The Hague. 1960, July 30, v. 13, No. 2, 121–32, 1 fig. [14 refs.]

A mycological survey of 572 cases of ringworm of various clinical types was carried out by the author in Lisbon. Routine methods used were: microscopical

examination of native material in 40% caustic potash solution, culture on Sabouraud's dextrose agar containing antibiotics and, when necessary for confirming identification of doubtful species, the various nutritional tests recommended by GEORG for this purpose.

Taken as a whole, results showed a high percentage of positive cultures and a wide variety of dermatophyte species as follows: *Trichophyton violaceum*, 27·9%; *Microsporum canis*, 21·4%; *T. tonsurans*, 14%; *T. mentagrophytes*, 11·7%; *T. megnini*, 8·3%; *Epidermophyton floccosum*, 6·3%; *T. rubrum*, 6%; *T. schoenleini*, 3·5%; *T. verrucosum*, 0·2%; and in addition to these dermatophytes there were: *Candida albicans*, 0·4%; and *Scopulariopsis*, 0·2%.

These data were also broken down to provide information as to the relative frequency of the various species in different sites of the body. Thus, the fungi occurring most frequently in these sites were: in the scalp, *T. violaceum* and *M. canis*; in the finger-nails, *T. violaceum*; in the toe-nails, *T. megnini* and *T. mentagrophytes*; the trunk and limbs (tinea corporis), *T. tonsurans*, *T. megnini* and *T. violaceum*, followed closely by *T. rubrum* and *M. canis*; in the beard area, *T. megnini*; and in the groin, *E. floccosum*, followed by *T. rubrum*; on the feet, *T. mentagrophytes*.

Many cases were also recorded in which infection involved multiple sites.

Outstanding features of this survey were the relatively large number of isolates of *T. megnini* and the isolation of *T. verrucosum* for the first time in Portugal.

C. J. La Touche

MARPLES, Mary J. **Recent Isolations of *Microsporum distortum* in New Zealand.** *J. Investigative Dermat.* 1960, June, v. 34, No. 6, 435–8, 1 fig.

Microsporum distortum which was first isolated and described by DI MENNA and MARPLES (*Trans. Brit. Mycol. Soc.*, 1954, v. 37, 372) has since then also been isolated in the United States of America from human and animal sources.

The author describes in this report 6 further cases of human infection (mainly in very young children) by this dermatophyte in New Zealand. Although she did not recover this species from the soil and although, in some cases at least, cats were probable transmitters of the infection, the author is of the opinion that its natural reservoir is probably the soil. *C. J. La Touche*

SALFELDER, K. Zur Differentialdiagnose der Histoplasmose. **[Differential Diagnosis of Histoplasmosis]** *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1960, v. 11, No. 4, 453–69, 17 figs. [Numerous refs.]

The English summary appended to the paper is as follows:—

"Difficulties encountered in the differential diagnosis of histoplasmosis—a fungus disease which is endemic in the U.S.A., Central and South America, and Africa—are discussed and two cases, which at first had not been definitely recognized as *Histoplasma capsulatum* infections, are reported.

"One case involved a generalized hematogenic histoplasmosis which had started from old primary foci in the hilar lymph nodes of the lungs attended by bilateral diffuse pneumonia. In the other case—a 113 days old girl—primary lesions of an early stage, caused by a not generalized histoplasmosis infection, were detected in the lungs. Also granulomatous tissue reactions entailing necroses were found in the foci of the lungs and in the lymph nodes, being specific in the latter.

"The Gomori-Methenamine-Silver technique and GRIDLEY'S staining method permit differential diagnosis of the Gram-positive fungi (*Histoplasma capsulatum*). In endemic areas, fibrin-positive granular formations which occur in specific and non-specific inflammations of the lungs and, obviously, have their origin in the exudate may be mistaken for *Histoplasma* infections."

SINN, C. M. **Amphotericin B in Bilateral Cavitary Histoplasmosis. Report of a Case with Two-Year Follow-up.** *J. Amer. Med. Ass.* 1960, July 16, v. 173, No. 11, 1220–22, 5 figs.

Chronic pulmonary histoplasmosis usually progresses slowly to a fatal termination. It is therefore very encouraging and of great interest to read of this reputed cure of a patient whose case is described by the author.

This patient was first seen in June 1957. She had a history of febrile illness and cough which had developed in January 1956. Haemoptysis caused her to seek medical advice, and as a result she was admitted to a tuberculosis sanatorium in March 1956. Examinations for organisms did not reveal any acid-fast bacilli despite repeated samples of sputum and gastric wash-outs, but *Histoplasma capsulatum* was obtained on culture. On X-ray examination "bilateral upper lobe disease with diffuse infiltration and cavitation" was found.

By June 1957, when she was re-admitted, her health had deteriorated very considerably with loss of weight to cachectic proportions. Despite intensive treatment which included blood transfusion, and the administration of vitamins and antibiotics, there was little improvement in the patient's condition until August 1957 when it was decided to initiate amphotericin B therapy by intravenous injection. Accordingly, over a period of about 4 months, she received about 90 intravenous injections of 50 mgm. each.

During this time of amphotericin B therapy the patient gained 28 lb. in weight and "cough and sputum diminished to an irreducible minimum"; moreover, X-ray examinations of the chest showed much improved lung fields, and six consecutive daily sputum specimens were negative for *H. capsulatum*.

2 years after the initiation of amphotericin B therapy this patient was carrying out normal domestic duties.

C. J. La Touche

KOSUNEN, T. **Experimental Monilial Infection in Mice. Virulence Studies.** *Ann. Med. Exper. et Biol. Fenniae.* Helsinki. 1960, v. 38, No. 4, 420–23.

"The virulence of seven *Candida albicans* strains was studied in mice inoculated by the intravenous route. 30 mice were challenged with each strain. The death rates

ranged from nil to seven with the various strains. The number of yeast cells in the kidneys was determined by the microbial enumeration method over a period of ten days. With all strains the microbial populations showed a tendency to increase but there were no significant differences in microbial counts between the strains."

LOURIA, D. B. **Specific and Non-Specific Immunity in Experimental Cryptococcosis in Mice.** *J. Exper. Med.* 1960, May 1, v. 111, No. 5, 643–65, 9 figs. [33 refs.]

The fatal nature of cryptococcosis in man is usually attributed to lack of antibody response to infection by *Cryptococcus neoformans.* It has however been demonstrated experimentally by BENHAM [see this *Bulletin*, 1957, v. 32, 206] that antibodies to cryptococci in rabbits could be produced after removing the capsule with hydrochloric acid [see also *ibid.*, 1950, v. 25, 756].

In the hope of further elucidating this problem, the author carried out a series of experiments in which mice were first inoculated with small numbers of *C. neoformans* and later challenged with a normally lethal inoculum of the same yeast.

The author also carried out control experiments in which normal mice were inoculated with small numbers of *C. neoformans.*

Results showed that the course of fatal cryptococcosis in mice could be modified by this type of immunization and that it appeared to be associated with a decrease in tissue fungal populations during the first 7 days after inoculation. This immunity was "species-specific and did not protect against heterologous challenge with *Staphylococcus aureus, Klebsiella pneumoniae* and *Mycobacterium tuberculosis.*"

When modification of fatal cryptococcosis was also achieved by inoculating mice with 100 to 200 μgm. of *Salmonella* endotoxin 7 days before challenge it was associated with only a minimal reduction in tissue fungal population.

As regards the control experiments, it was observed that the fungal populations in the tissues increased markedly during the first 7 days, although during the next 6 months they decreased.

The author considers that these results show that control of infection as indicated may be due to the development of specific antibody. *C. J. La Touche*

GRÄSSER, R. Pathogenitätsteste mit anaeroben Actinomyceten. [**Pathogenicity Tests with Anaerobic Actinomycetes**] *Zent. f. Bakt.* I. Abt. Orig. 1961, v. 181, No. 1, 103–10, 1 fig. [19 refs.]

The English summary appended to the paper is as follows:—

"Twenty eight actinomycetes strains of different origin were tested for their pathogenicity in Syrian hamsters. All of the eight strains of Act. israeli (KRUSE), isolated from typical cervico-facial actinomycosis of humans proved to be highly pathogenic to Syrian hamsters. Strains isolated one to one and a half years previously showed the same pathogenicity as recently isolated strains.

"It did not matter whether seven strains tested were injected in saline or in liquid medium. With one exception the 32 infected hamsters died from progressive actinomycosis. The mean survival time was three months.

"All other strains did not cause an infection. Even those strains which morphologically and culturally may be differentiated from Act. israeli (KRUSE) only with difficulty and which, in my opinion, are ecological variants of Act. israeli (KRUSE), and the strains pathogenic to swine and cattle did not cause any reactions in Syrian hamsters."

HIGGINS, E. S. **Metabolic Effects of *m*-Dinitrobenzene in *Aspergillus niger*.** *Proc. Soc. Exper. Biol. & Med.* 1960, Dec., v. 105, No. 3, 583–6. [11 refs.]

Communicable Diseases

The order in this section is:—**Tuberculosis; Venereal Diseases; General Infective Diseases; Other Communicable Diseases.**

For the bacteriology of these diseases see the section on Bacteriology below. For diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN

TUBERCULOSIS

STEWART, C. J. **Community X-Ray Surveys.** *Roy. Soc. Promotion Health J.* 1961, Jan.–Feb., v. 81, No. 1, 51–5, 1 fig. Discussion 55–6.

In 1957 it was decided to conduct X-ray surveys parish by parish throughout East Suffolk, England, with the object of eradicating tuberculosis in the county. Preliminary consultations were held with local councils in order to obtain their co-operation, and a canvass was organized to make a census of the population, to make an appointment for every adult to attend at a definite time and to persuade the hesitant or those who did not wish to attend.

Numerous and different factors were found to influence attendance. The more remote districts had better response rates than urban areas; the worst were the suburban areas

with little or no community life of their own. Details of percentage attendance are given. The rate was over 80% in 54 villages or towns and it fell below 50% in only 2.

At the end of 2½ years 43,753 adults (66% of those invited) had been X-rayed. 31 new cases of active tuberculosis (0·7 per 1,000 X-rayed) were discovered. A further 500 cases of healed tuberculosis were found (11·4 per 1,000). These patients have been kept under observation and already some have shown evidence of relapse requiring treatment. Generally there was a good attendance of both sexes in middle life but the young and the old were bad attenders.

The incidence of new cases discovered by the survey is about twice that of the normal clinic case-finding technique but fewer cases were discovered than would have been expected from the known incidence of the disease in the area.

STEWART asks whether it is desirable or necessary to prolong the survey or return later to discover the remaining cases of active tuberculosis. "The answer is probably 'No', although it is too early to reach a final decision." He also asks whether it is necessary to return to X-ray only adults over the age of 55 and to return to those villages with a low attendance or high incidence or both, or can the tuberculin testing of the schoolchildren be relied on to detect infection. He concludes that when an attendance of 70% is achieved probably only 1 X-ray survey will be necessary. *H. G. Calwell*

JONES, J. S. **An Investigation in Volunteers undergoing Mass-Radiography Examination in the City of Canterbury, 1958.** *Tubercle.* 1960, Dec., v. 41, No. 6, 441–7. [14 refs.]

During a 2-week mass radiography survey in the City of Canterbury in February 1958, a random sample of volunteers were asked a number of questions. This sample consisted of 922 people out of a total examined of 5,633. 77·4% said they had come as a simple precautionary measure. 10·8% for respiratory symptoms, 6·4% because they thought they were contacts. 57 (6·2%) were already attending their family doctor. Of 714 persons who said that they were being X-rayed as a simple precautionary measure 6·3% had respiratory symptoms, and 2·5% tuberculosis contact. Of the 208 persons seeking radiography for other reasons, 50·9% had respiratory symptoms, 28·4% had a history of tuberculosis contact, and 25·5% were already under their family doctor. 26·6% were attending for the first time, 43·6% for the second, and 29·8% for the third time or had previously attended even more frequently.

As a result of the whole survey, only 16 persons with abnormal radiographs were referred to the Canterbury Chest Clinic and only 1 case of carcinoma of the bronchus, and 1 case of pulmonary tuberculosis calling for close observation were detected. The author remarks, that there is no way of knowing how many patients with respiratory symptoms were probably given a false sense of security by being told they had a normal X-ray, thinking that this excluded serious respiratory disease or diseases of the heart. The author wonders whether mass X-ray examination as at present conducted is not outliving its useful purpose. *F. H. Young*

PRATT, P. C. & ATWELL, R. J. **The Diagnostic Reliability of Acid-Fast Bacilli demonstrated in Aspirated Gastric Contents.** *Amer. Rev. Respiratory Dis.* 1961, Jan., v. 83, No. 1, 96–9. [14 refs.]

"A series of specimens obtained by gastric aspiration from patients in a tuberculosis hospital has been examined for acid-fast bacilli by smear and culture.

"Most specimens which were positive for acid-fast bacilli on microscopy were also positive on culture; a few were negative on culture. The latter specimens were obtained from patients already being treated for proved tuberculosis. It may be concluded that the demonstration of acid-fast bacilli by microscopy of gastric aspirations from patients suspected of having pulmonary tuberculosis is as reliable for purposes of early diagnosis as demonstration in the sputum. Acid-fast bacilli other than *M. tuberculosis* were rarely found in smears of gastric aspirations. The smears of specimens from which unclassified mycobacteria were cultured were negative in all but one instance."

ELEY, A. J. & GOUGH, J. H. **An Investigation into the Reliability of Single Reading of Miniature Chest Films.** *Tubercle.* 1960, Dec., v. 41, No. 6, 435–40. [22 refs.]

This paper deals with the value of multiple mass X-ray readings. The paper commences by reviewing the literature on this subject which has now grown to considerable dimensions with much diversity of opinion. The Mass Miniature Radiography Unit maintained by the Ministry of Health at Tavistock Square, London, in the 5-year period June 1st, 1952, to May 30th, 1957, examined 220,000 individuals with a rejection rate for pulmonary tuberculosis of 0·77%.

34,000 men who had passed this screen entered the R.A.F. during this 5-year period. Within 2–3 months of the previous examination postero-anterior and lordotic views were taken on 35 mm. films. 27 individuals were rejected by the R.A.F. among those who had passed through the Ministry of Health unit. An elaborate re-investigation of these films was undertaken. In 1 individual the suspected lesion was not in the same zone as the tuberculosis lesion discovered 3 months later by the R.A.F., and in 1, the shadow found by the R.A.F. was found to be due to pneumonia. 15 were considered positive on the further review by the very strict criteria which had been arranged. 3 of those whose films were lost were added to this group, giving a total of 18 patients. The other 7 miniature films were still considered negative.

An attempt was made to follow-up all the patients in the positive group over a period of 2–7 years after they were discovered. Of the 15 patients 13 had quiescent disease, and 2 could not be traced. Of the 13 patients traced 7 had never received any treatment other than clinical supervision, 5 had chemotherapy alone, and 1 had a segmental resection. The result of this review was that only 4·57% of correct positive cases were added to those discovered by a single reading. It is clear, therefore, that in this series the advantages derived from a second reading were meagre. They have to be weighed against the disadvantages, including the recall of 30–50% more patients with negative films with consequent anxiety and

inconvenience, increased costs and administrative difficulties.

The authors conclude that in experienced hands, single reading of miniature films is adequate and double reading will reveal only a small proportion of additional cases with significant disease. *F. H. Young*

WARFVINGE, L. E. **A Comparison of Skin Tests performed simultaneously with Old Tuberculin and Endotuberculin in Active Pulmonary Tuberculosis.** *Acta Tuberculosea Scandinavica.* 1960, v. 39, No. 4, 286–96, 2 figs. [32 refs.]

This study is a contribution to knowledge of the specificity of a new type of tuberculin, Endotuberculin (ET) compared with OT in patients with active pulmonary tuberculosis.

474 patients from whom tubercle bacilli had been recovered were included in the study; they were divided by age into 2 groups, *viz.*, those born before 1900 (115 patients) and those born later (359 patients).

The OT used was the commercial product of a Stockholm laboratory and the ET was prepared by extraction from living bacteria alternatively frozen and thawed and filtration [this *Bulletin,* 1958, v. 33, 271]. [For previous work on similar lines with *Myco. tuberculosis* see GRASSET, *ibid.,* 1939, v. 14, 861.]

By comparative Mantoux tests in man and animals it was found that a dry substance content per 0·1 ml. of 2, 7 and 18 μgm. of ET corresponded approximately to 1, 10 and 100 TU of OT.

Testing was begun with 1 TU of OT and 2 μgm. of ET injected into the skin of either arm simultaneously. If no induration occurred on the 3rd day or it was less than 5 mm., higher doses were given, OT 10 and 100 TU respectively, ET 7 and 18 μgm. until a reaction was obtained or the subject was found to be a non-reactor.

In the group of 115 older patients the mean diameters of reaction to the 1st, 2nd and 3rd tests with OT were 12·2, 12·7 and 17·5 mm. and with ET 11·7, 13·6 and 12·8 mm. In the group of 359 younger patients the diameters with OT were 11·3, 13·3 and 17·8 mm. and with ET 11·1, 13·4 and 7·2 mm. (4 patients only).

Percentage reactors and accumulated percentage reactors *

	OT			ET		
	Dose	Percentage reactors	Accumul. percentage reactors	Dose in μgm.	Percentage reactors	Accumul. percentage reactors
Group I: 115 patients born before 1900						
1st test	1 TU	30·4	—	2	67·0	—
2nd test	10 TU	62·5	73·9	7	71·1	90·4
3rd test	100 TU	75·9	93·7	18	80·0	98·3
Group II: 359 patients born in 1900 or later						
1st test	1 TU	36·5	—	2	76·9	—
2nd test	10 TU	79·6	87·0	7	95·2	98·9
3rd test	100 TU	93·2	99·4	18	75·0	99·7

* According to the formula:

$$p_1 + p_2\,(1-p_1) + p_3\,[1-(p_1+p_2(1-p_1))].$$

It was thus seen that the mean diameters of induration with 1st and 2nd doses of OT and ET were within the same range in both age-groups but with the 3rd dose OT in both groups gave much bigger reactions than ET.

Analysis of reactor rates showed that in both age-groups ET gave twice as many reactors to the 1st dose and also a higher accumulated reactor rate. It was therefore more specific and more sensitive. The higher specificity of ET was also shown by the finding that in the old-age group the accumulated reactor rate was 98·3% compared with 93·7% with OT.

The demonstrated superiority of ET in older people is of special interest when it is considered that with increasing age there is some decline in tuberculin sensitivity [*ibid.,* 1958, v. 33, 832] and with an increasing incidence of tuberculosis in later life it is of great importance to have a tuberculin that works well in the elderly.

A possible explanation of the different reactivity between OT and ET could be the presence of heat-labile fractions in ET which have been destroyed in heated preparations like OT and PPD. *H. G. Calwell*

MACPHERSON, A. Margaret C., ZORAB, P. A. & REID, Lynne. **Collapse of the Lung associated with Primary Tuberculosis. A Review of 51 Cases.** *Thorax.* 1960, Dec., v. 15, No. 4, 346–54, 4 figs. [20 refs.]

This paper continues and amplifies the previous study on the same subject (*Thorax,* 1950, v. 5, 1). It deals with 51 children who showed radiological evidence of segmental or lobar lesions suggesting a reduction in lung volume and who had positive tuberculin tests. They were selected from 1,323 patients attending the Brompton Hospital contact clinic, London, between 1932 and 1957; the average follow-up period was 12 years. In 40 of the 51 patients hilar glands were visible and in 11 glandular enlargement was not evident although the parenchymatous lesions still remained. As the majority of the children had contracted tuberculosis before the advent of chemotherapy few were treated by this method and the observations on this were too few to be of value. The children received institutional treatment. It is considered that when there is a primary tuberculous affection severe enough to cause a segmental lesion a period of rest and observation is beneficial and this is best carried out in an institution. Of the 15 children whose chest radiographs cleared, only one child was treated at home and 14 in hospital; whereas of the 36 children whose radiographs never returned to normal, 14 had been treated at home during the active stages of the disease.

Radiographic clearing does not necessarily imply that the underlying lung is histologically normal. In 17 instances out of the 59 lesions which occurred in 51 children, complete radiographic clearing of the pulmonary lesions had occurred within 6 months from the time they were first diagnosed. After a further 6 months another 7 had cleared, making a total of 24 during the first year. After this only 6 further patients showed complete clearing.

34 out of the 51 children were between 1 and 6 years of age; infants were not often seen in this clinic as they usually went to paediatric clinics.

Of the 59 initial lesions, 20 appeared in the right upper lobe, and 18 in the right middle lobe. The lower lobes

were less commonly affected; the prognosis for these is not good for it was seen that of 13 lower lesions only 5 showed recovery. In 5 children surgical treatment was required for relief of symptoms resulting from lower lobe lesions.

Bronchography and bronchoscopy were not carried out as a routine measure, but the details of those patients who had these investigations performed are given. 7 patients required resection of one or more lobes of the lungs; details and radiographs of these patients are given. Only one of these patients died, this followed an accident. The nature of the lung shadows and their pathology are discussed. The majority of children with active primary lesions associated with radiographic changes suggesting a reduction in lung volume recover clinically and active tuberculous pulmonary lesions seldom develop. The policy of using general medical and antituberculous measures rather than thoracotomy and removal of glands in the early stage has been successful in 41 out of the 51 children.

The authors consider that having had the opportunity of observing these children over a long period, only the cases of obstruction of the trachea or large bronchi require urgent removal of caseous glands and they think that the policy of maintaining an expectant attitude is justified.

F. H. Young

PAUL, R. **Investigation of Unexplained Pleural Effusions in Africans.** *Tubercle.* 1960, Dec., v. 41, No. 6, 430–34. [12 refs.]

During the past 10 years, over 100,000 African workers in the copper mines in Northern Rhodesia have undergone routine clinical and X-ray examination on entry to employment and annually thereafter. The most common abnormality seen was pleural thickening.

Pleural thickening is often due to previous pleural effusion and the high incidence in Africans raises the question of its aetiology. There is a widely held opinion that the condition is most commonly tuberculous but the authors' observations did not support this view and they therefore began an enquiry into the frequency of tuberculosis as a cause of pleural effusion.

42 patients with pleural effusion were followed up for 2–10 years. Their average age was higher than that of the group in which tuberculosis is common. 24 of the patients had no symptoms, and 18 had pain in the chest with or without unproductive cough. The mean erythrocyte sedimentation rate was 49 mm. in 1 hour (Westergren), all had sputa negative for tubercle bacilli, none received any form of treatment, and in all cases the fluid was absorbed leaving pleural thickening in 33. [There is no mention of the tuberculin state.] The average period of follow-up of the whole group was 4·6 years; pulmonary tuberculosis developed in 2 (5%).

In a series of 17,697 African workers it was found that the incidence of pleural thickening was only 1½ times greater in the reactors to tuberculin than in the non-reactors; 16·5% of those with pleural thickening were non-reactors. This suggests that a proportion of effusions leading to pleural thickening are not due to tuberculosis.

The pleural fluid was studied in 47 Africans with effusion. In all cases the sputum was negative for tubercle bacilli, and 8 patients were non-reactors to tuberculin and in them the effusions were unlikely to be tuberculous. A preponderance of lymphocytes was found in 30 (64%) of the fluids, which would support a probable tuberculous aetiology but it should be noted that 4 of the 8 non-reactors had lymphocytic fluid which is against a tuberculous aetiology. Culture yielded tubercle bacilli from 8 (17%) of the 47 fluids, and all 8 patients were reactors.

These findings cast doubt on the validity of the opinion that the majority of pleural effusions in Africans are tuberculous. No other specific aetiological factor has yet been discovered but investigation will be continued.

H. G. Calwell

THOMAS, H. E., FORBES, D. E. P., LUNTZ, G. R. W. N., ROSS, H. J. T., SMITH, J. M. & SPRINGETT, V. H. **100% Sputum-Conversion in Newly Diagnosed Pulmonary Tuberculosis.** *Lancet.* 1960, Nov. 26, 1185–6, 1 fig. [11 refs.]

This paper reports sputum conversion results on 1,000 newly diagnosed patients admitted to the Birmingham Hospitals between January 1st, 1957 and December 31st, 1958. Positive sputa were obtained from 545 of these patients. 3 patients whose bacilli were resistant to 2 drugs and 12 who died were excluded—only 5 of these died of tuberculosis. A table showing types of resistance is given and included 528 (96·9%) whose bacilli were sensitive to all drugs.

At the end of 1 month 84% of those on therapy by standard drugs had produced their last positive sputum; at the end of 6 months only 2·3% had not achieved conversion, and at the end of 10 months the sputum of all patients had become completely negative. Details of the method used to test resistance are given, and a short discussion on the results reported by other workers follows [see also this *Bulletin*, 1959, v. 34, 1099; 1960, v. 35, 134, 562].

F. H. Young

WILLIAMS, A. W. **East African Tuberculosis Therapy Trials—a Review.** *East African Med. J.* 1960, Dec., v. 37, No. 12, 743–64. [50 refs.]

Clinical therapeutic trials have become an established procedure, and in particular trials in which several hospitals participate but which are co-ordinated and planned from one centre. This enables a larger number of comparable cases to be admitted to the trial in a reasonable time. The Medical Research Council ranks high among those who have evolved and refined these trials.

In this review Professor Williams describes the various Tuberculosis Therapy trials carried out in East Africa, with planning and direction shared between the Tuberculosis Research Unit of the MRC and the Department of Medicine, Makerere College, and with various centres in the three East African territories collaborating.

There have been 5 of these investigations so far, and 2 more have just commenced [see, for example, this *Bulletin*, 1956, v. 31, 902; 1957, v. 32, 422; 1959, v. 34, 749; 1960, v. 35, 663, 986].

The first in 1953–5 compared African patients treated with either isoniazid and streptomycin (SH) or isoniazid and para-aminosalicylic acid (PH) with radiographically

matched patients from previous MRC tuberculosis trials in England. This established that such trials could be undertaken and that African patients responded to chemotherapy in a similar way to European patients in England.

Further trials were then designed to test other drugs than streptomycin or PAS for use with isoniazid as neither of these is entirely suitable for mass out-patient treatment. The second trial in 1956 compared the combination of diamino-diphenyl sulphone 100 mgm. plus isoniazid 200 mgm. daily (DH) with the standard treatment of PAS 10 gm. plus isoniazid 200 mgm. (10 PH). These patients were treated for 6 months in hospital and followed up for 1 year. The trial showed clearly that the sulphone was not effective in preventing the occurrence of isoniazid-resistant strains, and that the results were similar to those which might be expected with isoniazid alone.

A third pilot trial for 3 months only in 1957 suggested that a combination of thiacetazone (TB1) 150 mgm. with isoniazid 200 mgm. might well prove effective.

The fourth trial in 1957–8 was designed to test further the effectiveness of isoniazid alone in a dosage of 200 mgm. (H), isoniazid in high dosage, 20 mgm. per kgm., combined with pyridoxine (to prevent neuritic complications) (HIP), and the standard 10 PH. In this trial the patients were treated for 1 year in hospital. The trial showed that though in clinical and radiological results the 10 PH régime was slightly more effective, in bacteriological results it was much superior. 96% of the 10 PH cases were bacteriologically negative at the end of the year on direct smear, and 84% negative on culture. 81% of the HIP cases were negative on direct smear, and 67% on culture. Only 67% of the H cases were negative on direct smear and 57% on culture. Even more important was the fact that all the positive cultures, considerable in number in the isoniazid only series, were resistant to isoniazid.

The fifth trial in 1958–9 compared the combination of thiacetazone 150 mgm. plus isoniazid 200 mgm. (TB1/H), a combination of another anti-leprosy drug diphenylthiourea 2 gm. with isoniazid 200 mgm. (DPT/H), and the standard 10 PH. The patients were treated for 6 months in hospital and 6 months more as out-patients. The DPT/H combination was not effective, but the TB1/H seemed to be as effective as 10 PH in producing negative sputum cultures, and preventing isoniazid resistance. Overall assessment including clinical and radiological progress suggested that TB1/H was almost as satisfactory as 10 PH but that there was evidence of toxicity in some cases.

The current trials are designed to test various dosage combinations of thiacetazone and isoniazid to see which are most effective and least toxic both under hospital and domiciliary treatment conditions.

Thiacetazone and isoniazid can be given combined in a small tablet twice daily, and the cost is but a fraction of the PAS and isoniazid whether given separately or in cachets.

Details are given as to the design and organization of the trials, the type of disease and the selection of patients, the duration of treatment and observation, the bacteriological and radiological methods and criteria, and the implications and applications of the results. [It is not possible to abstract all this, and those interested are recommended to read the original which is in itself a summary of several papers.] *A. C. E. Cole*

East African/British Medical Research Council: **Thiacetazone/Diphenylthiourea Investigation. Comparative Trial of Isoniazid in Combination with Thiacetazone or a Substituted Diphenylthiourea (SU1906) or PAS in the Treatment of Acute Pulmonary Tuberculosis in East Africans. A Co-operative Investigation in East African Hospitals and Laboratories with the collaboration of the British Medical Research Council.** *Tubercle.* 1960, Dec., v. 41, No. 6, 399–423. [20 refs.]

This trial was made in hospitals in Kenya, Tanganyika and Uganda in order to explore the possibility of using drugs other than streptomycin and PAS along with isoniazid in the treatment of pulmonary tuberculosis in those countries. PAS has the disadvantage of being bulky and expensive, and streptomycin is also expensive and unsuitable for widespread daily use in poor communities. The drugs chosen for the trial were thiacetazone (*p*-acetamidobenzaldehyde thiosemicarbazone) and a substituted diphenylthiourea, the thiocarbanilide SU1906.

All the patients in the trial were indigenous Africans aged 15 years or more with newly diagnosed, untreated, acute, extensive and rapidly progressive pulmonary tuberculosis believed to be of recent origin, and with a positive sputum. The method of selection and allocation to a regimen was the same as that used in the East African and British Medical Research Council Isoniazid Investigation (1960) [this *Bulletin*, 1960, v. 35, 986] except that patients with unilateral disease were eligible for the present trial.

174 patients were allocated to a treatment regimen between August 1958 and February 1959 of whom 156 remained for analysis. The 3 regimens studied were:

1. TB1/H—Isoniazid 200 mgm. daily with thiacetazone (TB1) 150 mgm. daily in 2 equal doses given by mouth at an interval of about 12 hours.
2. DPT/H—Isoniazid 200 mgm. daily with SU1906 (DPT) 2 gm. daily as above.
3. 10 PH—Isoniazid 200 mgm. daily with sodium PAS 10 gm. daily as above.

The chemotherapy was prescribed for 1 year, the first 6 months in hospital and the 2nd 6 months as out-patient treatment. During the 1st 3 months rest in bed was prescribed but later the amount of rest was left to the physician's discretion. All collapse therapy was withheld during the year of chemotherapy but postural therapy was permitted. The circumstances in which the regimen could be changed were laid down in the conditions of the trial. They included major uncontrollable toxic reactions and serious radiographic deterioration.

There were more males than females in all 3 series but otherwise there was reasonable similarity for example as regards age, clinical state and radiographic and bacteriological assessment.

In the main analysis of 127 patients it was found that there was 1 early tuberculous death in the TB1/H series, 1 non-tuberculous death in the DPT/H series and 2 early deaths in the 10 PH series, 1 due to tuberculosis and 1 to acute necrosis of the liver attributed to PAS.

Substantial clinical and radiographic progress was made in all 3 series. In the patients in the main analysis at the end of 6 months negative culture results were obtained

in 77% of the TB1/H, 51% of the DPT/H and 87% of the 10 PH series. At 12 months the corresponding figures were 87% in the TB1/H and 88% in the 10 PH series. Isoniazid-resistant strains were found at 6 months in 29, 51 and 16% of the patients in the respective groups.

In the 29 patients with initially resistant organisms 7 of the 8 TB1/H patients had negative cultures at or before 12 months, and 8 of the 12 10 PH group had negative cultures at or before 12 months.

4 of the total of 51 patients in the TB1/H group had toxic reactions necessitating change of treatment, 3 of the 55 DPT/H patients and 2 of the 50 10 PH patients also had severe toxic reactions.

The status of all patients at 12 months, based primarily on bacteriological results was assessed as favourable in 72% of the TB1/H group, 79% of the 10 PH group, doubtful in 7% and 5% respectively and unfavourable in 21% and 16% respectively.

It was concluded that thiacetazone, 150 mgm. daily, is of similar efficacy to sodium PAS, 10 gm. daily, as a companion for isoniazid, 200 mgm. daily, in producing sputum conversion and preventing the emergence of resistant strains. A pilot trial included in the main trial showed that a dose of 200 mgm. of thiacetazone was more toxic than the smaller dose. Further trials are going on to discover the lowest effective dose of thiacetazone.

H. G. Calwell

SHARIFF, A. K. **Ambulatory Chemotherapy in Pulmonary Tuberculosis.** *Pakistan J. of Health.* 1960, Oct., v. 10, No. 3, 192–7.

The ambulatory treatment of tuberculosis is of special importance in under-developed countries where tuberculosis is prevalent and hospital accommodation insufficient.

This paper presents the results obtained in Karachi [population 1,126,417], Pakistan, in 1953–55 in 2,349 patients treated for pulmonary tuberculosis at the Tuberculosis Control and Training Centre.

Stage of Disease	*No.*	*No. with positive sputum*	*No. with sputum conversion*	*No. Improved*
		Males		
Minimal	174	56	18 (32·1%)	76 (43·6%)
Moderate	706	558	160 (28·6%)	340 (44·4%)
Advanced	290	264	52 (19·6%)	97 (33·4%)
Total	1,170	878	230 (26·2%)	487 (41·6%)
		Females		
Minimal	278	116	77 (66·3%)	171 (61·5%)
Moderate	687	478	201 (40·2%)	427 (62·1%)
Advanced	214	183	38 (20·7%)	108 (50·4%)
Total	1,179	777	316 (41·1%)	706 (60%)

[One set of these figures do not add up correctly.]

It is thus seen that 41·6% of males and 60% of females improved and there was sputum conversion in 26·2 and 41·1% respectively. The more favourable results in female patients may be due to the fact that the number of females with minimal disease was more than 1½ times the number of males although the total number of either sex was about the same. Another factor may have been the economic conditions in which if the breadwinner is the patient he often has to continue at work even when acutely ill.

Domiciliary chemotherapy would achieve satisfactory results if it were properly organized along with home nursing care (which was not available in Karachi), if search were made for early cases and if there were a health insurance scheme.

H. G. Calwell

LOTTE, A. & ROUILLON, A. Enquête sur la chimioprophylaxie et la chimiothérapie précoce des tuberculoses primaires de l'enfant et de l'adolescent. Résultats immédiats et éloignés (1953–1959). [**Study of Chemoprophylaxis and Early Chemotherapy of Primary Tuberculosis in Children and Adolescents. Short-Term and Long-Term Results**] *Bull. Inst. Nat. Hyg.* Paris. 1960, Sept.–Oct., v. 15, No. 5, 713–832, 7 figs.

This study reports the results of an enquiry into the value of chemo-prophylactic treatment of patients who had become infected with tuberculosis within the year preceding treatment.

The patients were divided into 3 groups by age:—less than 5 years, 5 to 9 years, and 10 to 24 years; and into 4 categories according to the type of response to the infection: These were 1. patients without clinical or radiological disease; 2, 3, 4. patients with only radiological evidence of abnormalities of glands or pulmonary tissue (group 2), with clinical symptoms only (group 3), and those with clinical and radiological signs (group 4).

The patients were divided into 2 sections, those untreated with drugs, and those treated by drugs given daily (isoniazid 20 mgm./kgm. before the age of 2 years, and 10 mgm./kgm. for those over 2 years, with PAS 300 mgm./kgm. with a maximum of 15 gm. daily). Drug treatment was carried out for a minimum of 6 months and usually longer. Other methods of treatment and régimes were the same in both sections. The selection of patients for the 2 sections was satisfactory with the exception that a larger number of the more serious cases were in the treated group. 4,557 patients were studied. Of these 1,267 were in category 1, of whom 116 had drug treatment. Of the 3,290 who fell into the other categories, 1,702 were, and 1,588 were not treated by drugs.

The following conclusions were apparent:—A definite improvement followed drug therapy in the categories showing obvious disease, especially in the reduction of post-primary development though it had little effect on the development of bronchial obstruction which was conditioned more by the age of the patient, and the nature of the gland at the start of treatment. During an observation period of 1–5 years there was marked reduction in the appearance of haematogenous lesions in young children, and phthisis in older children and young adults.

Apart from bronchial obstruction, morbidity was reduced by the use of drugs, in patients observed for 1–5 years, from 9% to 1% in children under 5 years old, from 9% to 2% in children aged 5–9, and from 13% to 2% in subjects aged 10–24. In the 1st (latent) category there was

a considerable reduction of morbidity, but the numbers were insufficient for statistical analysis.

This excellent paper is supported by a wealth of statistical tables. *F. H. Young*

MOORE, W. **Stevens-Johnson Syndrome, Erythema Multiforme Pluriorificalis, in association with the Administration of Thiosemicarbasone.** *Tubercle.* 1960, Dec., v. 41, No. 6, 448–9.

This report illustrates an unusual toxic manifestation due to thiosemicarbazone (TB1, thiacetazone). A young man aged 26 who had pulmonary tuberculosis was treated by the 3 orthodox drugs in hospital for 3 months. On his discharge, thiacetazone was substituted for PAS in doses of 100 mgm. twice daily together with isoniazid 150 mgm. twice daily. On the 25th day after starting the thiacetazone he returned to hospital extremely ill. His eyelids were swollen and there was a profuse purulent discharge from his eyes. His lips were cracked and bleeding and there was a general oozing from the gums. He had sore throat and dysphagia. He was covered with a generalized haemorrhagic rash mainly on the chest, back and upper extremities. No visible changes in the rectum or anus and no retinal haemorrhages were seen. A blood film was well within normal limits. Drugs were immediately stopped, and at the end of 14 days his condition had practically resolved itself. A few days later treatment was resumed with small doses of thiacetazone gradually increased until at the end of 2 weeks a dose of 100 mgm. daily had been reached. Recurrence of the symptoms then occurred.

Desensitization by corticotrophin [GUPTA and PALMER, this *Bulletin*, 1959, v. 34, 878] was successful and at the time of the report the patient had been treated with a daily dose of thiacetazone 200 mgm. with isoniazid for 4½ months without further incident. *F. H. Young*

SCHÜTZ, Ingeborg. Über die Behandlung der kavernösen Lungentuberkulose mit Aethioniamid. [**The Treatment of Cavitating Pulmonary Tuberculosis with Ethionamide**] *Deut. med. Woch.* 1961, Jan. 20, v. 86, No. 3, 133–9, 2 figs. [31 refs.]

Ethionamide (2–ethylisonicotinthioamide) has been used by the author in the treatment of pulmonary tuberculosis since February 1959. A total of 113 patients received the drug, and its therapeutic effect has been assessed in 50.

The duration of treatment was less than 1 month in 37 patients, 1–2 months in 39, 2–3 months in 23 and over 3 months in 14. The various regimens used were: ethionamide, 4 patients; ethionamide with thiosemicarbazone, 5; ethionamide with cycloserine, 88; ethionamide with PAS, 1; ethionamide with streptomycin, 1 and ethionamide with various drugs 14.

The 50 patients whose progress was analysed in detail were all treated with ethionamide and cycloserine except 1 who received PAS. The usual daily dose of each drug was 1 gm., and when PAS was used its dose was 12 gm. daily. All had positive sputa at the start of the treatment, and all had received some form of chemotherapy earlier. 24 had isoniazid-resistant organisms, 15 had organisms resistant to streptomycin and isoniazid, and 2 had streptomycin-resistant strains. The bacilli in the remaining 9 patients were fully sensitive both to isoniazid and streptomycin.

46 patients had thick-walled cavities; these measured 4 cm. and over in 24; 26 were expectorating tubercle bacilli copiously. After 2 months' treatment there was shrinkage of cavities in 37 patients (reduction to ½ or more in 20), no change was seen in 10, and there was increase in 3. There was thus improvement in 74% of the patients. Tubercle bacilli could not be found in direct examination in 51% and by culture in 40%.

In spite of combined treatment 5 of 20 patients had organisms resistant to ethionamide after 1 month, and after 2 months almost one half of the still positive cultures showed resistant strains. In 4 patients with positive cultures after more than 3 months' treatment all strains were resistant to ethionamide.

Later results were equally disappointing. 6 patients were treated for 6 months to 1 year without success. All relapsed after early improvement. It was found, however, that whereas sputum conversion and shrinkage of cavities occurred in only 39% of 18 patients with advanced disease there was sputum conversion in 85% and shrinkage in 50% of 14 patients with less advanced disease.

45 (40%) of the 113 patients complained of side effects of the treatment, and it had to be stopped prematurely in 24 (21%). There was diminished appetite in 29, abdominal pain in 13, vomiting in 11, nausea in 7 and urticaria in 1.

Of the 88 patients who received ethionamide with cycloserine 35% complained of side effects which the author attributed mostly to cycloserine. These included headache, giddiness, excitability, convulsions and tiredness. Cycloserine had to be withdrawn in 11·5%. *H. G. Calwell*

EDGE, J. R. & WEBER, J. C. P. **Ethionamide (1314TH) and Viomycin in the Treatment of Resistant Pulmonary Tuberculosis.** *Tubercle.* 1960, Dec., v. 41, No. 6, 424–9.

14 patients with very chronic cavitating pulmonary tuberculosis from organisms resistant to all 3 standard antibacterial agents were treated with ethionamide (1314 TH) [this *Bulletin*, 1959, v. 34, 620] 1 gm. daily, and viomycin also 1 gm. daily, as far as was possible. Although clinical and radiological changes are reported the report deals with the effect on the sputum. The 14 were divided into 3 groups: (1) Inconclusive: of the 4 in this group 3 patients died before the end of 3 months treatment, and in 1 treatment had to be stopped because of the incidence of jaundice. (2) 5 patients were classified as failures. In 3 treatment had to be stopped because of toxic manifestations either to the ethionamide or the viomycin, and in 2 the sputum remained positive. (3) 5 patients were thought to have been successfully treated; 1 became sputum-negative but relapsed owing to refusal of further treatment. In 1, startling improvement occurred, and the sputum became consistently negative, but the patient died of amyloid disease; a second had a sputum conversion, but he also died of amyloid disease. In 2 negative sputum was obtained and maintained for 18 and 8 months respectively. Brief case histories are given and the results are tabulated.

The authors consider that ethionamide with viomycin has a definite place in treatment, though some disappointment was experienced with the use of viomycin 1 gm, owing to the development of nerve deafness in 3 and vestibular symptoms in 1 patient. *F. H. Young*

BONSTEIN, H., ROSSI, G., FRIEDRICH, T., LAUENER, H., AGUET, M. & FAVEZ, G. Influence de l'apport de pyridoxine sur l'activité des transaminases chez les tuberculeux traités par l'isoniazide à doses élevées. **[Influence of Pyridoxine Administration on the Transaminase Activity on Tuberculous Patients Treated with Isoniazid in High Dosage]** *Schweiz. med. Woch.* 1961, Feb. 4, v. 91, No. 5, 134–41, 4 figs. [35 refs.]

The English summary appended to the paper is as follows:—

"22 tuberculous patients divided into two equal groups were treated for 3 months with a daily therapy schedule of 600 mg of INH, 12 g of calcium benzoyl-PAS, streptomycin and, in the first few weeks, corticosteroids as well. One of the groups also received 30 mg of pyridoxine hydrochloride daily. Besides the usual tests, neurological examinations and determinations of the glutamic-oxaloacetic-transaminase (GOT) values in blood and serum were carried out.

"The antituberculous drugs were well tolerated and no neurological disorders could be discovered in the 22 patients. The therapeutic results were good in both groups, considering the uneven distribution of exudative cases. There was a drop in the blood GOT values in the patients treated by high doses of INH without vitamin B_6. On the other hand, enzymatic activity increased in patients receiving pyridoxine. Serum GOT values showed less uniform variations. During corticosteroid therapy, a rise in the transaminase values was observed. It may be concluded from this study that during prolonged INH treatment with a daily dose of 10 mg/kg, the administration of 30 mg of pyridoxine per day is more than enough to prevent a latent vitamin B_6 deficiency."

DAHLSTRÖM, G. & UGGLA, L. G. Corticosteroider och tuberkulos. **[Corticosteroids and Tuberculosis]** *Opuscula Med.* Stockholm. 1961, Jan., v. 6, No. 1, 24–7, 3 figs.

The English summary appended to the paper is as follows:—

"Three cases are described in which generalized tuberculosis developed during the treatment with corticosteroids. Miliary tuberculosis of the lungs was found after 8 months use of corticosteroids in a 67-year-old man with malignant lymphogranulomatosis. The other two patients who both suffered from disseminated lupus erythematodes developed tuberculosis in other organs (spleen, kidneys, a joint) as well as miliary lung changes. One of them, a 71-year-old woman, had been treated with corticosteroids for about four years and a normal pulmonary X-ray had been found four months before tuberculosis was diagnosed. In the other case, a 47-year-old woman, the corticosteroid treatment had lasted 1½ years. On the basis of these and other cases it is suggested that a prophylatic use of antituberculous drugs might be tried in connection with longlasting corticosteroid treatment."

JESIOTR, M. **[Combined Treatment of Superficial Tuberculous Lymph Nodes with Steroids and Antibiotics]** *Harefuah.* Jerusalem. 1961, Jan. 15, v. 60, No. 2, [in Hebrew 47–9, 6 figs. English summary 49].

The English summary appended to the paper is as follows:—

"Treatment of superficial tuberculous lymph nodes with steroids in addition to antimicrobial treatment, brings about a more rapid and stable recovery than previous therapy.

"Although steroids are usually applied locally, in bilateral far advanced cases the treatment is also general. Duration of treatment with steroids is 4–6 weeks. Antimicrobial treatment is prolonged up to 2 years. We found no complications in connection with this treatment. Only in cases with extremely destructive changes within the lymph nodes is resection indicated, and this only after the aforementioned treatment which lessens markedly the area of operation."

WALLGREN, A. Einige Probleme der Calmetteschen Impfung. **[Some Problems of BCG Immunization]** *Deut. med. Woch.* 1961, Jan. 20, v. 86, No. 3, 105–11.

This address was given to a meeting of paediatricians in Brunswick in May 1960.

There are now on record 9 cases of fatal BCG vaccination—5 in Scandinavia, 1 in Austria and 3 in Chile. 8 of the patients were children and 1 was an adult. There was no evidence of the BCG having regained virulence, and it is presumed that the vaccinated persons had an unexplained lack of resistance to the organism. It is therefore no longer justifiable to claim that BCG vaccination is a universally harmless procedure, and it is necessary to compare the risk of vaccination with the risk of contracting tuberculosis.

The connexion, if any, between BCG vaccination and sarcoidosis is discussed briefly. The majority of those vaccinated with BCG in Sweden are children but sarcoidosis is rarely seen in a child. The aetiology of sarcoidosis is still obscure, and the occurrence of the condition in a vaccinated person is no proof of a connexion.

The truth about the value of BCG vaccination does not lie either with the enthusiasts and optimists who believe that it can speedily eradicate tuberculosis or with the sceptics and pessimists who believe it to be entirely worthless.

Wallgren has never expected greater protection from vaccination than from natural primary infection. Both afford some immunity against superinfection or a new primary infection. It cannot be claimed that a vaccinated

person will never develop tuberculosis, but there is no infallible vaccination procedure in any field of medicine.

The results of the British Medical Research Council's Tuberculosis Vaccination Trial which began in 1950 and were last reported on in 1959 show a reduction in tuberculosis morbidity in the vaccinated group of schoolchildren of not less than 83%. Wallgren accepts this trial as being beyond statistical or other reproach. Protection was demonstrated against both primary and post-primary tuberculosis. Generalized tuberculosis and meningitis occurred only in the unvaccinated group.

Wallgren is not worried by the loss of the tuberculin test in diagnosis. Tuberculin sensitivity in Swedish children is nearly always due to vaccination but there are other methods available by which the diagnosis may be made in the rare cases of tuberculosis in childhood.

The last problem discussed is that of vaccination policy and programmes. There is no problem where non-reactors who are in danger of exposure to tuberculous infection are concerned. All should be vaccinated whether children or adults. In addition mass vaccination of non-reactors is indicated in countries with a high rate of tuberculosis morbidity and the earlier in life vaccination is done the better. Routine BCG vaccination of the newborn has been practised in Sweden for the past 30 years.

Whether or not routine vaccination of the newborn is advisable depends on the natural reactor rate in children entering school. The rate at 7 years in Sweden is "a few" per cent; and in Wallgren s opinion the time has come to curtail or discontinue the routine vaccination of the newborn in that country. No general rule can be laid down but perhaps the decline of the natural reactor rate at school entry to 10% should cause those concerned to take stock of their vaccination programme.

If mass vaccination of the newborn is not indicated it is unlikely that there will be any need for mass vaccination of schoolchildren before the age of puberty either. The matter is otherwise, however, where older children are concerned for they are likely to be exposed to tuberculous infection in their wider environment after leaving school. Mass vaccination of children in the age-group 10–11 is therefore advisable, and is likely to be continued in Sweden for a long time to come.

Mass vaccination of the newborn continues in Sweden and tuberculin sensitivity persists during school life in 90% of the children. Tuberculosis morbidity in infants and young children is now almost nil, mostly because of the control of infection in the community and little, Wallgren thinks, because of vaccination.

The decision was taken in 1958 to continue mass vaccination of the newborn and to test all schoolchildren aged 10–11 years with tuberculin and to vaccinate or revaccinate all non-reactors. This decision was accepted by all health authorities in the country. Further review is to take place shortly when it may be found that there is no longer any need for mass vaccination of the newborn. Vaccination of schoolchildren as above is still indicated and of all specially exposed persons. "For all ages, however, the best weapon against tuberculosis is the absolute prevention of infection by the tubercle bacillus."

H. G. Calwell

CERF, J., DARRAS, T. & LEBRUN, A. Premiers résultats de la vaccination BCG indiscriminée à Léopoldville. **[First Results of Mass BCG Vaccination without Preliminary Tuberculin Testing in Léopoldville]** *Ann. Soc. Belge de Méd. Trop.* 1960, June 30, v. 40, No. 3, 457–68.

Mass BCG vaccination without preliminary tuberculin testing was begun in Léopoldville (Congo) in April 1957. Freeze-dried vaccine (0·1 mgm.) was given by intracutaneous injection, care being taken to protect it against heat and light before use.

The incidence of glandular abscess after vaccination was very low, but this favourable result cannot be attributed to weakness of the vaccine as the tuberculin conversion rate in a sample group of 800 children aged 6-14 years was 92%. The expected natural reactor rate in such a group would have been 25%.

The vaccinal lesions measured 4·5 mm. in the youngest children and 5·5 mm. in older children, owing to the higher incidence of the Koch phenomenon with increasing age. These measurements compare favourably with that of 4·9 mm. reported in Danish non-reactor children vaccinated with 0·075 mgm. of BCG.

One cause of the low complication rate is the fact that in Léopoldville it is not usual for mothers to bring their infants for routine medical examination (including vaccination) before the age of 6 months. In the present tuberculosis situation in the Congo the authors do not think that BCG vaccination at birth is required.

The results of post-vaccinal tests were:—

	Interval after vaccination	Number	Percentage of BCG tests positive	Percentage of tests with 100 TU of OT positive
I	2½ months	1,750	95	80
II	8 months	800	—	87
III	12 months	1,746	47	45
IV	24 months	790	43	41

It was seen that the reasonably high conversion rate immediately after vaccination (corrected for estimated rate of natural tuberculin sensitivity) was only maintained for 8 months and fell markedly thereafter.

At the time of writing 75% of the 360,000 African inhabitants of Léopoldville had been vaccinated with BCG as described during a period of 3 years in which the medico-social environment had changed little except for the vaccination campaign. In 1957 the discovered incidence of tuberculosis was 8 per 1,000 in the general population, nil in infants and 4–5 in children aged 6–14 years. In 1959 the rates were 3·6, nil and 0·66 (3 cases) respectively. The favourable effect was seen in adults and children and both primary and post-primary disease were reduced.

The authors conclude that in the prevailing conditions of work mass BCG vaccination without preliminary tuberculin testing is the only preventive measure against tuberculosis that can be applied on the necessary scale. The BCG test is preferable to the tuberculin test after vaccination as it not only detects allergy but, if living BCG is used, reinforces vaccination. Revaccination is recommended after 12 months and again at intervals not yet determined.

H. G. Calwell

VENEREAL DISEASES

PUB. HEALTH REP. Wash. 1960, Nov., v. 75, No. 11, 989–99, 6 figs. **A Current Look at Venereal Diseases. [i]. Current Status of Syphilis in the United States** [BROWN, W. J.], 990–93. **[ii]. Case-finding in Chicago** [WACTOR, P. R., Jr.], 993–7. **[iii]. New Haven's Court Clinic: a Casefinding Source** [BOHAN, G. N.], 997–9.

i. In 1959, 120,000 cases of syphilis in civilians were reported in U.S.A.: 8,200 of these were infectious. Reported cases of early syphilis fell rapidly from 1950 to 1955, remained steady till 1958 and then rose; the reservoir of untreated syphilis at the present time is estimated to be 1,200,000 and the annual incidence 60,000. There are 33,000 paretics in institutions, and they cost 48 million dollars a year, but deaths from syphilis have dropped from 14,000 to 4,000 a year and infant deaths from syphilis from 574 to fewer than 1 per 100,000 live births.

The difficulty of getting private physicians to report cases is being overcome; in Louisiana, Pennsylvania and Kansas reporting has increased 10 times or more and in 1959 49% of patients were interviewed for sex contacts.

It is not known whether the increase of known cases of syphilis is absolute or relative, but though incidence has probably increased, it does seem that better reporting is the major factor, from the figures quoted. These are set out in 6 figures. It seems probable that morbidity figures will rise, but in the long run further epidemiological effort will help toward eradication.

ii. This article describes the activities of the Municipal Social Hygiene Centre, Chicago, gives a number of statistics and includes a mild panegyric of the chief medical officers. Since 1938 it has dealt with 3 million persons and in its files since 1934 are records of 800,000 male and 700,000 female patients; 5,200 patients attend each month and in a year 16,000 cases of gonorrhoea and as many as 7,083 of syphilis are treated. Interviewers are all male including 4 "peppy epi" boys (epidemiological staff); in the first half of 1959 there were 48 "source patients" with infectious syphilis and in the same period of 1960 there were 169; a house-to-house survey brought in 465 patients (23 with infectious syphilis) out of 4,338 reactors [what these latter were is not clear].

In recent times difficulties have arisen: (1) hospitals send in reports of positive reactors only once a month, (2) syphilitics often have few symptoms [? signs], (3) doctors tend to have a low index of suspicion of venereal disease, and (4) the tendency of men and boys to associate with their own sex. A table gives details of the 48 source-patients in 1959 and of the 169 in 1960, number of names obtained, located, syphilis, treated, contact-index, etc.

An investigator interviews about 100 patients a month and of 10,134 persons named, 6,000 were brought in in 6 months; at the County Jail 50–100 rapid reagin tests are carried out each day and 8.5% prove syphilitic. The number of examinations rose from 43,787 in 1956 to 122,169 in 1959 and the number treated rose from 5,951 to 7,608; the number of infections rose from 21,635 in 1956 to 23,361 in 1959 including 16,102 cases of gonorrhoea, 7,083 of syphilis and 61 of other venereal diseases. Of the syphilitic patients in 1959, 746 were primary or secondary, 1,154 early latent, 4,843 latent and 340 congenital; 1,701 were private patients and 5,382 from institutions.

iii. In New Haven, Connecticut, every effort is being made to find sources of venereal disease; all positive laboratory findings must be reported, *e.g.* positive serum tests for syphilis, finding gonococci, etc. To supplement this a "court clinic" was set up in September 1942; to this are referred all persons arrested on vice charges for examination for venereal disease. The examination includes a blood test for syphilis, cultures and smears for gonococci (routinely in women and in men when indicated) and a physical examination. All patients found to have venereal disease are followed up and contacts are traced; the patient can choose between treatment at the clinic or by a private physician. From 1943 to 1959 4,733 persons were examined; 413 (8·7%) were found to have syphilis and 280 (5·9%) had gonorrhoea; all were treated. Of the other two compulsory examinations, 400,392 pre-marital blood tests gave only 3,679 (0·9%) positive results and 361,538 pre-natal tests 0·4%. *T. E. Osmond*

BOUISSET, L., RUFFIE, J., DUCOS, J. & CIRERA, P. Sur la fréquence de la syphilis dans certaines populations de l'Ouest Saharien. **[The Frequency of Syphilis in Certain Populations of the West Sahara]** *Bull. Soc. Path. Exot.* 1960, July–Aug., v. 53, No. 4, 616–20.

These authors tested 515 sera by means of the Kolmer, Kline and VDRL tests using cardiolipin antigen.

69 specimens came from the Tadjacan tribes, a previously nomadic people who have lived sedentary lives since the 2nd century in the oasis of Tindouf; they live poor lives.

401 came from Réguibat, Saharan nomads who move about over vast areas from South Morocco to Mauritania. 45 came from various clans or tribes.

10·14% of the 69, 1·25% of the 401 and 6·67% of the 45 gave positive reactions; the results with the 3 types of test agreed closely.

In spite of the fact that the sedentary tribesmen were under medical control they showed 10 times the amount of syphilis shown by the true nomads. The explanation appears to be that the true nomads live in small communities each of only a few tents which have few if any dealings with one another whereas the sedentary ones mix freely. *T. E. Osmond*

RANQUE, J., RUFFIE, J., DUCOS, J. & MOULIN, J. Sérologie syphiligraphique des autochtones du Borkou-Tibesti. **[Syphilis Serology of the Indigenous People of Borkou-Tibesti]** *Bull. Soc. Path. Exot.* 1960, July–Aug., v. 53, No. 4, 650–56.

These authors tested the blood of 222 of the African population of this area and of 114 soldiers (Sarah) of the garrison of Faya-Largeau by means of the Kahn and

Kline VDRL tests: 7·2% (16) of the former and 10·4% (12) of the latter were positive. These figures were considerably lower than those of other observers in Bechuanaland which varied from 30 to 37%. Syphilis therefore does not seem to be widespread in the oases of Borkou or Tibesti and there is no appreciable difference in its incidence between nomads and sedentary persons. [This is in complete contrast to what was recorded in the previous article (see above).] *T. E. Osmond*

Boiron, H., Castets, M., Plagnol, H., Lambert, F. & Mallet, M. Une nouvelle preuve de la spécificité des tests au cardiolipide dans de diagnostic sérologique de la syphilis. **[A New Proof of the Specificity of Cardiolipin Tests in the Sero-Diagnosis of Syphilis]** *Bull. et Mém. École Nat. Méd. Pharm. de Dakar.* 1959, v. 7, 218–21. [14 refs.]

It has been stated that a disequilibrium of the blood proteins in the African may cause false positive serum reactions for syphilis when cardiolipin antigen is employed. In order to disprove this these authors tested (1) 159 specimens of cord blood of new-born infants, (2) 18 from the superior longitudinal sinus of children of 1–4 months, (3) 58 from children aged 6 months to 6 years, (4) 113 from schoolchildren aged 6 to 16 years, (5) 54 from young persons aged 17 to 21 years, and (6) 182 from adults aged 25 to 42 years (total 584).

In group (1) there were 7 positive results but none of these infants showed any signs of congenital syphilis, (2) 18 tests of the above 7 all became negative in less than 4 months, (3) all 58 were negative, (4) 1 was positive: this child showed clinical evidence of congenital syphilis and the parents gave a history of syphilis, (5) 5 positive reactions were obtained (2 probably syphilitic), (6) 21 (11.5%) gave positive reactions.

Hyperglobulinaemia reaches its peak level chiefly in the age groups 6–7 years whereas the most positive reactions were in the age group over 17: this is said to prove that cardiolipin tests are specific. *T. E. Osmond*

Pariser, H. **Sensitivity of Reiter Protein Complement Fixation and Standard Serologic Tests: Comparison and Correlation with Clinical Findings in Syphilis.** *Southern Med. J.* 1960, Dec., v. 53, No. 12, 1543–9. [14 refs.]

This article reports the results of testing 500 sera in parallel by the Reiter protein complement-fixation test (RPCF) and the Kolmer and VDRL quantitative reactions (STS) and correlating them with the clinical findings. Of 10 cases of untreated primary syphilis, 3 were non-reactive with both types of test, 4 were reactive with both and 3 were reactive with STS only. Of 33 cases of untreated secondary syphilis 2 were reactive only with STS and 1 was non-reactive with both tests; of sera tested after treatment 2 were reactive with STS but not with RPCF. It appears that RPCF tends to become reactive later than STS but remains reactive longer.

After treatment, 173 tests carried out on 89 patients showed 26 reactive with RPCF and non-reactive with STS but only 3 showed the opposite. In addition 13 cerebrospinal fluids from adequately treated early syphilis were all negative with RPCF [as would be expected].

47 cerebrospinal fluids from patients with paresis or meningovascular syphilis adequately treated were also tested; both types of test remained reactive for long periods but tended to weaken slowly, and there was no marked difference in results; as has been noted in the past the status of the cerebrospinal fluid bore no fixed relation to that of the blood.

Thus the RPCF appears to be somewhat less sensitive than STS but possibly more specific; only if its sensitivity can be increased should it replace STS. The use of both tests seems advisable at the present time.

Details of 42 cases with pre- and post-treatment results are set out in a table. *T. E. Osmond*

Thivolet, J., Grospiron, D. & Murat, M. Mise en évidence, par les techniques d'immunofluorescence, d'anticorps au cours de l'infection syphilitique. **[Demonstration, by means of Immunofluorescence, of Antibodies in the Course of Syphilitic Infection]** *Ann. Inst. Pasteur.* 1960, Dec., v. 99, No. 6, 920–24.

Whatever antigen may be present, 2 methods are available to demonstrate antibodies to it: (A) The serum to be tested, and then an animal anti-globulin human fluorescent serum are placed on fixed treponemes. If the serum contains antibodies they are fixed on the treponemes and shown up by the fluorescent anti-globulin serum which renders the treponemes fluorescent. Thus positive sera provoke fluorescence. (B) The test serum and then a fluorescent human syphilitic serum are placed onto treponemes; thus the treponemes are only rendered fluorescent if the original serum does not contain antibodies susceptible of blocking their antigenic attachment. With technique (A) these authors noted (1) a feeble non-specific fluorescence, (2) a specific fluorescence of moderate intensity, (3) irregular reproducibility.

The authors' results are set out in a table which it is difficult to understand but it seems that fluorescent tests agreed fairly well with TPI but were rather more often positive (88 against 73 in all syphilitics and 72 against 57 in treated cases); classical serum tests and TPCF gave several false positives and were less sensitive.

However, it seems to be difficult to produce a satisfactory technique and further work is necessary.
T. E. Osmond

Alergant, C. D. **Tabetic Spinal Arthropathy. Two Cases with Motor Symptoms due to Root Compression.** *Brit. J. Venereal Dis.* 1960, Dec., v. 36, No. 4, 261–5, 4 figs.

Sylvestre, L., Bélanger, M. & Gallai, Z. **Urogenital Trichomoniasis in the Male: Review of the Literature and Report on Treatment of 37 Patients by a New Nitroimidazole Derivative (Flagyl).** *Canadian Med. Ass. J.* 1960, Dec. 3, v. 83, No. 23, 1195–9. [80 refs.]

The history of the discovery of *Trichonomas vaginalis* (TV), a description of the parasite, the incidence of infection, methods of transmission, clinical signs and laboratory diagnosis are set out in some detail [all of which can

be found in any good text book]. There is also a very complete bibliography. The reported incidence in the male (urethritis) varies from 5·5% to 68·0% [but few will believe the latter figure].

An account of various remedies used in treatment by various authors shows that none was effective until Flagyl was tried; this substance is L-(2'hydroxethyl)-2-methyl-5-nitro-imidazole, also known as RP 8823.

These authors treated 37 male patients suffering from prostatitis or urethritis or both with 250 mgm. of Flagyl twice daily for 10 days and obtained cure in all: 10 of these patients were followed up for 12 weeks or more. No side effects were noted.

The authors stress the importance of prostatitis in the male and of treating both partners when one is found to be infected. [See also this *Bulletin*, 1961, v. 36, 145, 146.]

T. E. Osmond

CSONKA, G. W., LITCHFIELD, J. W., OATES, J. K. & WILLCOX, R. R. **Cardiac Lesions in Reiter's Disease.** *Brit. Med. J.* 1961, Jan. 28, 243–7, 7 figs. [19 refs.]

These authors describe 3 male cases of Reiter's disease in which cardiac involvement occurred, and one of a woman in whom the diagnosis was doubtful. A review of the literature shows that in the past various observers had described cases which showed abnormal cardiac signs and symptoms including pericarditis.

Of the 3 patients one showed urethritis, arthritis and conjunctivitis followed by enlargement of the heart with a prolonged P–R interval and a high sedimentation rate; a year later he had a relapse (or reinfection). The second patient contracted gonorrhoea and non-gonococcal urethritis followed by arthritis, iritis and aortic incompetence with enlargement of the heart: the sedimentation rate was increased and the P–R interval 0·28 second; he recovered but vision was very poor. The third patient had non-gonococcal urethritis, arthritis and iritis; these were followed by signs of aortic incompetence with a P–R interval of 0·24 second; joint changes are shown in 3 figures. A fourth case—of a woman—showed iritis, aortic regurgitation and arthritis; pathological investigations gave results similar to those in the males; the patient died of heart failure. At autopsy the arteries showed arteritis and lymphocytic infiltration and the cervix was eroded.

[Since this condition may follow bacillary dysentery, non-specific diarrhoea or venereal urethritis it seems that the term Reiter's syndrome is preferable to Reiter's disease as recommended by BARON (*Brit. Med. J.*, 1961, v. 1, 426).]

T. E. Osmond

GENERAL INFECTIVE DISEASES

The order in this section is:—**General; Hospital and other Cross Infections; Coccal Infections; Bacterial Infections; Virus Infections.**

GENERAL

GREGERSEN, G. Et 15-Års meningitis materiale pa et centralsygehus. En efterundersögelse. [**15 Years of Meningitis Material at a Central Hospital. A Follow-up Investigation**] *Ugeskr. f. Laeger.* 1961, Jan. 27, v. 123, No. 4, 123–9, 2 figs.

During the last 20 years there has been a gradual improvement in the immediate prognosis for purulent meningitis. Little is known about the ultimate prognosis with regard to the survivors after such meningitis. To throw light on this subject, a follow-up study was undertaken of the patients treated at the Randers Central Hospital during the last 15 years. During the period 1945–1959 a total of 736 patients were treated, 144 for purulent, 569 for serous, and 23 for tuberculous meningitis. After subtraction of the 84 who died in immediate connexion with their meningitis, there remained 652 to whom a questionary was sent requiring information on the following subjects:—paralyses, convulsions, deafness, giddiness, impaired mental faculties or delayed development, disturbances of vision, hydrocephalus, and any other condition capable of association with the meningitis. On this score data were collected in 570 cases (a response of 87·4%). Among the tuberculous meningitis patients there were only 2 survivors. About 50% of the survivors of purulent meningitis still presented symptoms referable to it. With the passage of years, this percentage fell to 25. About 33% of the survivors of serous meningitis still presented symptoms of it, and here again with the lapse of time this percentage fell to 25. Only in 7 of the 570 answers did they refer to such serious sequels as hydrocephalus, blindness, total deafness, etc. Most of the symptoms were slight and often reminiscent of the post-traumatic brain syndrome. Classification of the patients according to their age failed to demonstrate significant differences in the frequency of symptoms in this respect.

Claude Lillingston

DIAMANT, M., EK, S., KALLOS, P. & RUBENSOHN, G. Gammaglobulinbehandling och infektionsskydd. [**Gamma Globulin Treatment and Protection against Infection**] *Svenska Läkartidningen.* 1960, Dec. 16, v. 57, No. 51, 3575–89, 5 figs.

Children aged 1 to 7 years admitted to hospital for acute otitis during a year and a half since February 1958 served as material for a controlled test of gamma globulin, which was or was not given according to whether their birthdays fell on odd or even days. Thus 113 received it while 118 did not, the treatment they received otherwise being approximately the same. It was given on admission to hospital and thereafter at monthly intervals, the dosage being 0·6 ml. of a 12% solution per kgm. body weight. The analyses previously undertaken showed a serum content of gamma globulin normal for children at various ages. The efficacy of the treatment given was gauged by counts of the recurrences of otitis. Not only were the

recurrences twice as frequent in the controls as in the treated cases, but multiple recurrences in individual cases were most numerous in the former, with up to 5 recurrences in the same case, but never more than 2 each in the treated cases. In both groups of cases the recurrence rate was highest about 2 months after the onset of otitis, and the risk of a first attack of recurrence was 1·5% for the treated cases as compared with about 3% for the untreated controls. It is argued that gamma globulin may be given for recurrent otitis, particularly in the case of children.

Claude Lillingston

JÄNNES, L., KOSUNEN, T. & LEISTI, P. **Two Combined Pertussis-Diphtheria-Tetanus Prophylactics. A Comparative Study with Different Contents of Diphtheria Toxoid and Adjuvant.** *Ann. Med. Exper. et Biol. Fenniae.* Helsinki. 1960, v. 38, No. 3, 252–5, 2 figs.

Although it is recognized that reactions to triple antigen vaccine are most probably due to the pertussis component, the authors wondered if reduction of the diptheria antigen and the mineral adjuvant might decrease the number of local reactions without diminishing the protection given against diphtheria. 12 children (3–12 months old) were given two 0·5 ml. doses of standard Finland vaccine [50 Lf doses of diphtheria toxoid, 10 Lf doses of tetanus toxoid, the equivalent of 20,000 million pertussis bacteria and 10 mg. aluminium phosphate (*i.e.*, 2.2 mgm. of Al), per ml.] with an interval of 5 weeks. 17 children of the same age were similarly injected with a triple vaccine containing only 25 Lf doses of diphtheria toxoid and 5 mgm. of aluminium phosphate per ml.: otherwise both prophylactics were identical and all 4 components were taken from the same batches: both toxoids were highly purified. Examination of the diphtheria antitoxin levels 6 weeks after the second injection showed that there was no significant difference between the 2 groups. The number of vaccinated children in this trial was too small to determine the effect of dilution of the diphtheria toxoid and mineral adjuvant on the number and nature of untoward vaccination reactions.

D. A. Cannon

HOSPITAL AND OTHER CROSS INFECTIONS

ROBINSON, S. S., GOLEY, A. F., BRUTON, O. C. & BAKER, H. J. **A Nursery Epidemic of Staphylococcic Infection.** *U.S. Armed Forces Med. J.* 1960, Dec., v. 11, No. 12, 1415–22, 2 figs.

An epidemic of staphylococcal skin infection in the maternity unit of the Walter Reed Hospital between November 1958 and April 1959 is described.

The infection rate in January was 19%, and between November and early February 39 infants were infected, 28 of them with a strain of phage type 52/44A/42B/81 [it is not clear what phages were used to type these strains but it is possible that they are the same as strains typing 52/80/81 in Britain]. As mothers and babies tend to leave hospital earlier in the United States than in Britain many of these lesions were detected at the post-natal visit.

Nasal and rectal swabs were taken from the occupants and staff of the unit. 7 of the 17 infants in the single nursery were carriers of the epidemic type, as were 4 of the 5 nurses and 2 of the 29 other personnel. The epidemic type was also recovered from plates exposed in the nursery and in the hall near the outlet of the nursery exhaust fan.

At the beginning of February control measures were started. All nasal carriers of the epidemic type were treated with neomycin-bacitracin cream, and a plastic face shield was used by carrier nurses while attending infants. The use of penicillin and streptomycin was restricted and frequent hand washing with pHisoHex [hexachlorophene with pHisoderm, a preparation of cholesterols and other substances] was encouraged. Individual plastic aprons were provided for each baby to be worn by any nurse attending the infant.

Babies who were carriers were discharged and intensive laboratory checks on infants and personnel for the following 3 months showed that nurses did not become recolonized and no infant was subsequently colonized with the epidemic type. There were no more staphylococcal lesions. [There were presumably no breast abscesses or other maternal lesions in this epidemic.]

M. Patricia Jevons

SCATENA, L., COSTA, A., PINTO, F. H. & BARACCHINI, O. *Staphylococcus pyogenes* resistentes a antibióticos isolados do naso-faringe de recém-nascidos. [**Isolation of Antibiotic Resistant *Staphylococcus pyogenes* from the Nasopharynx of Newborn Infants**] *Rev. Inst. Adolfo Lutz.* S. Paulo. 1959, v. 19, 69–73. [12 refs.]

The English summary appended to the paper is as follows:—

"Working with material collected from the nose and pharynx of fifty newborn babies (four days old), the authors isolated antibiotic resistant *Staphylococcus pyogenes* in 22 cases, 44% of the infants.

"All Staphylococci isolated were resistant to penicillin, and almost all were resistant to streptomycin, chlortetracycline, and oxytetracycline.

"The results showed that there were antibiotic resistant *Staphylococcus pyogenes* in the nursery of the Clinical Hospital of the Medical School of Ribeirão Preto.

"The authors suggest that the nursery can be a possible source of Staphylococci infections in which penicillin, streptomycin, chlortetracycline are not effective."

BIRO, L., BUCHBINDER, L., GOLDBERG, S., PELLITTERI, O. J. & GIBBS, R. C. **A Staphylococcal Disease Outbreak in a Dermatologic Service. Bacteriological Studies; Effect of Prior Systemic Therapy.** *Arch. Dermat.* 1960, Nov., v. 82, No. 5, 740–45.

A bacteriological study was made in a dermatological ward that had been the seat of an outbreak of infection with staphylococci of phage type 80/81 for several months. 100 patients and 98 staff had nasal cultures examined on 1 or more occasions. Of 75 patients examined more than once, 15 developed staphylococcal

disease and 5 of them died; 11 yielded type 80/81 staphylococci. The deaths were all in patients with severe skin disease (3 pemphigus vulgaris, 1 mycosis fungoides and 1 histiocytosis). Of 38 patients followed from admission to discharge, 10 developed some staphylococcal disease. There were 7 cases of type 80/81 infection; in all cases the patients became nasal carriers of this strain before the development of the disease.

All the 15 patients developing staphylococcal disease had had antibiotic or steroid treatment, representing 48% of the 31 so treated; none of the 44 not so treated developed disease. It did not seem that the severity of the skin disease played a great part in determining the appearance of infection.

The epidemic strain of staphylococcus was found quite widely distributed in fomites in the 2 wards in which almost all the cases occurred. Carriers were rare among the staff and among those patients who did not develop disease.

The epidemic ceased after the institution of rigorous isolation for infected patients and increased attention to aseptic precautions generally. *R. E. O. Williams*

FINEGOLD, S. M. & GAYLOR, D. W. **Enterocolitis due to Phage Type 54 Staphylococci resistant to Kanamycin, Neomycin, Paromomycin and Chloramphenicol.** *New England J. of Med.* 1960, Dec. 1, v. 263, No. 22, 1110–16. [30 refs.]

During a 9-month period 8 cases of staphylococcal enteritis were encountered in a hospital in which there was an epidemic of staphylococcal disease due to a strain of phage type 54 resistant to penicillin, streptomycin, tetracycline, kanamycin, neomycin, paromomycin and chloramphenicol but sensitive to vancomycin.

All these patients had been given one or more of the following antibiotics usually by oral administration, before recovery of the staphylococcus from the stool:—chloramphenicol, kanamycin, neomycin, penicillin, tetracycline and sulphamethoxypyridazine, for bowel "sterilization", hepatic coma or intestinal infection.

5 of the 8 patients died, enterocolitis being the primary cause in 2. The enteritis subsided spontaneously in 2 cases after antibiotics were stopped and it was cured by vancomycin in 1. Vancomycin also controlled the bowel infection of 3 patients but they subsequently died from other causes.

The authors stress the dangers of the pre-operative bowel sterilization [especially by antibiotics to which the hospital epidemic strain is known to be resistant] and point out the use of vancomycin in the management of these cases. Detailed case-histories are given.

M. Patricia Jevons

SANSOTTA, S. & NOFRI, R. Stafilococchi chemio-antibiotico-resistenti isolati nel personale di assistenza degli Spedali Riuniti di Arezzo. [**Staphylococci Resistant to Chemotherapy and Antibiotics Isolated from Staff of the United Hospitals in Arezzo**] *Riv. Italiana d'Igiene.* 1960, Sept.–Oct., v. 20, Nos. 9/10, 324–32. [22 refs.] English summary (8 lines).

JENNISON, R. F. & KOMROWER, G. M. **Effect of an Antibacterial Nasal Cream on Nasal Colonization and Infection in the Newborn.** *Brit. Med. J.* 1961, Jan. 14, 89–92, 2 figs. [27 refs.]

A trial of the daily application of neomycin-chlorhexidine (Naseptin) nasal cream to mothers and babies was carried out in a maternity unit in an attempt to reduce staphylococcal carriage rate and sepsis. Infants were nursed in nurseries holding up to 15 cots. No other special measures were taken and masks were not worn by staff or mothers. Umbilical cords, however, were dressed twice daily with 1% chlorhexidine in spirit.

Naseptin was used on 113 babies, 132 infants were untreated and served as the control group. [It is not stated how infants were allotted to the 2 groups or if they were nursed in a separate nursery.] Swabs were taken within 24 hours of birth and at 4 and 8 days.

Coagulase-positive staphylococci were isolated from 2·5% of babies at the first swabbing. This figure rose to 50% and 67% in the control group at 4 and 8 days respectively. Only 18% of treated babies were colonized by the 8th day. The carriage rate of mothers was 29%; this was unchanged in the control group but fell to 3·2% on discharge in the treated group.

In the control group 11·6% infants had some form of infection in hospital and 23·5% of those who were followed-up reported some infection after returning home. Only 7·4% of treated babies were infected in hospital and 12·4% developed lesions later. There were fewer cases of staphylococcal conjunctivitis in the treated babies and cases were twice as common in carriers than non-carriers. Of the 6 breast abscesses which occurred 5 were in the control group and 4 of the babies were carriers on discharge. *M. Patricia Jevons*

KRUGMAN, S. & WARD, R. **Infectious Diseases of Children. 2nd Edition.**

This book was reviewed on p. 419.

COCCAL INFECTIONS

The order in this section is:—***Staphylococcus, Streptococcus, Neisseria, Others.***

FABER, V., JESSEN, O., ROSENDAL, K. & ERIKSEN, K. R. **Staphylococcal Bacteraemia. Clinical and Bacteriological Observations in 201 Cases.** *Brit. Med. J.* 1960, Dec. 24, 1832–6, 1 chart. [22 refs.]

Since 1953 the number of cases of staphylococcal bacteraemia diagnosed in the State Serum Institute, Copenhagen, which serves hospitals throughout Denmark, has risen from about 40 to nearly 100 per year whereas the total number of blood cultures submitted only increased from about 6,000 to about 8,000. An analysis is presented of the 201 cases diagnosed in 1957 and 1958.

41% of the patients died, the mortality rate being higher in the older patients. 124 of the patients were males. One-third had severe illnesses, including diabetes (21 cases), generalized skin disease (15) and blood diseases (11). 17 had had steroid treatment.

The origin of the infection could be inferred in 182 cases. 94 patients were probably infected in hospital and 88 elsewhere. In 51 cases the bacteraemia seemed to be derived from an operation site (including infusion, haemodialysis, etc.); in 64 it arose from boils, etc., and in 11 from the respiratory tract; the origins were various or unknown in the remainder.

87 of 222 staphylococci isolated from the 201 patients were phage type 80 or 52/52A/80. The mortality for 59 patients infected only with type 80 was 54%; for 24 with type 52/52A/80 it was 33%; and for 98 with other types, 39%. The mortality was higher in patients infected with antibiotic-resistant strains than in those with sensitive strains; it was also higher when the infecting strain failed to produce the egg-yolk (EY) reaction, and this association was only partly due to the fact that EY negative strains were generally resistant to antibiotics. [See also JESSEN *et al.*, this *Bulletin*, 1960, v. 35, 914.]

R. E. O. Williams

HALBERT, S. P., DI SANT'AGNESE, P. A. & KOTEK, F. R. **Staphylococcal Antibodies in Cystic Fibrosis of the Pancreas.** *Pediatrics.* Springfield, Ill. 1960, Nov., v. 26, No. 5, 792–9, 6 figs. [24 refs.]

Staphylococci are frequently cultured from the nose, throat and lungs of patients with cystic fibrosis of the pancreas. This could mean that they are merely present in increased number and frequency, or that they are actually involved in the pathogenesis of the lung lesions. An investigation was therefore made of staphylococci antibodies in such patients. The sera of 45 of them were compared with the sera of 49 control subjects admitted to the same hospital with other diseases. The two groups were similar in age, with a range from 1 to 22 years. The agar precipitin technique of antigen-antibody reaction was used.

More numerous and frequent antibody responses to the extracellular products of *staphylococcus aureus* were obtained in the sera of patients with cystic fibrosis than in the control sera. A similar result was obtained with extracts of a *Haemophilus influenzae* strain, but not with extracts of a haemolytic streptococcus—the latter possibly because of frequent and prolonged antibiotic prophylaxis in these patients. The organisms most to be feared in this disease would thus seem to be *Staph. aureus* and *H. influenzae.*

H. Stanley Banks

AARSKOG, D. & BASSÖE, H. H. **Vancomycin Treatment of Staphylococcal Pneumonia in a Patient with Low Resistance.** *Antibiotic Med.* New York. 1960, Dec., v. 7, No. 12, 782–3.

"A patient with low resistance was successfully treated with vancomycin for a staphylococcal pneumonia, after failure of erythromycin in doses which gave bactericidal serum concentrations when tested in vitro."

COBURN, A. F. **The Continuous Association of Poverty with Intensity of Rheumatic Manifestations.** *Amer. J. Med. Sci.* 1960, Dec., v. 240, No. 6, 687–700, 5 figs. [36 refs.]

Many countries have noted a decrease in the incidence and severity of rheumatic fever. This could be due to a change in prevalence or quality of an unknown determinant factor of some strains of group A streptococci or to improvement in general living standards. That florid and fulminating rheumatic fever can still occur is illustrated by the presentation in this paper of the details of 2 cases in indigent Puerto Rican families in New York. The author, after discussing many earlier papers on the association of rheumatic fever and poverty, suggests that the critical factor associated with poverty may be nutrition in early life.

M. D. Warren

BACTERIAL INFECTIONS

The order in this section is:—***General, Corynebacterium, Haemophilus, Enteric bacteria, Brucella, Pasteurella, Bacillus, Anaerobes, Spirochaetes, Others.***

EISLER, M. & TEICHMANN, J. Versuche über Simultanimpfung gegen Diphtherie und Tetanus. **[Experiments on Simultaneous Inoculation against Diphtheria and Tetanus]** *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1960, Nov., v. 120, No. 4, 249–52. [12 refs.]

Experimental observations are recorded on the effect on the immunity developed on injecting bacterial toxoid and antiserum simultaneously. The observations were made with alum-adsorbed toxoids and diphtheria, tetanus and staphylococcal antisera or with tetanus toxoid and the same antisera. The result of these observations was to show that at the end of 4 weeks the protection from diphtheria toxin was least in the group receiving diphtheria toxoid and diphtheria antiserum, in which 90% of the animals died, whereas in the groups receiving the other antisera or toxoid alone the death rate ranged from 50 to 55%. In the case of immunization with tetanus toxoid protection followed similar lines. Most animals died from a dose of tetanus toxin after 4 weeks in the group which had received toxoid and anti-tetanus serum, whereas in the group receiving tetanus toxoid and anti-diphtheria serum the results were better than in the controls which had received only toxoid.

The authors argue that this can only mean disintegration of the alum toxoid in the body and its neutralization by specific antibody. They admit that other workers on the same ground have obtained different results.

J. W. McLeod

STRÖM, J. **Is Universal Vaccination against Pertussis always Justified?** *Brit. Med. J.* 1960, Oct. 22, 1184–6. [23 refs.]

The author has drawn attention to the incidence of neurological complications after pertussis vaccination

occurring in many countries, and deals with the problem in Sweden in greater detail. During 1955–58 the incidence in Sweden was 1 in 6,000 and most of the neurological complications consisted of convulsions, coma or collapse with subsequent recovery, but there were 4 deaths and 9 cases indicative of encephalopathies with severe lesions (1/17,000). An investigation of the incidence of neurological complications after whooping cough showed that this was not as high as after vaccination. In 1955 the mortality rate in Sweden from whooping cough was 1 per million per annum, which was much less than the average for 28 other countries (18 per million per annum), and there were signs that the disease was also of a much milder nature than in previous years. On the basis of these observations the author's question seems justified.

F. T. Perkins

HOLDSWORTH, D. E. ***Hemophilus influenzae* Meningitis in an Adult. Report of a Case.** *Arch. Intern. Med.* 1960, Nov., v. 106, No. 5, 653–6, 1 graph.

A case of *Haemophilus influenzae* meningitis in a 63-year-old woman is reported. The onset is described, not very accurately, as "atypical", presumably because disorientation and semi-coma appeared as early as the 3rd day of symptoms. The organisms seen in a green-stained film of the spinal fluid on admission were erroneously thought to be pneumococci, and the patient was accordingly treated with large doses of penicillin and a sulphonamide, hydrocortisone being added because of her "critical state". When, by culture of the blood and spinal fluid, the organism was found to be *H. influenzae*, the treatment was not changed, but was supplemented by chloramphenicol. The patient responded rapidly within the next 2 days, but except for withdrawal of the hydrocortisone the polypharmacy, which included corticotrophin was continued for 4 or 5 days. A side effect of the steroid treatment was gastro-intestinal bleeding on the 5th hospital day. This is believed to be the 36th case of *H. influenzae* meningitis in an adult reported in the literature. [Cases like this are not uncommon, and there seems to be no particular reason why they should be reported, or why they should be so overtreated when it has been known for more than 10 years that chloramphenicol alone gives superb results in *H. influenzae* meningitis.]

H. Stanley Banks

CHASSAGNE, P. & GAIGNOUX, Y. Étude épidémiologique des infections typho-paratyphoïdiques en France, en 1958 et 1959. **[Epidemiological Study of Typhoid and Paratyphoid Infections in France in 1958 and 1959]** *Bull. Inst. Nat. Hyg.* Paris. 1960, Sept.–Oct., v. 15, No. 5, 881–911

This is a report on the epidemiology of typhoid and paratyphoid infections in France compiled by the National Institute of Hygiene; the data are set out in 22 tables. The number of cases reported in 1958 and 1959 (around 2,000 in each year) was about half of that reported in the immediately preceding few years. The origin of the infection in the 993 epidemiological notifications was discovered in less than 50%. The main sources of contamination were drinking water, vegetables, and shellfish. Contaminated wells played a smaller part than in previous years. Of the 125 cases attributed to drinking water in which the infecting organism was found, it was *Salmonella-typhi* in 69 (55%) and *Salm.-paratyphi B* in 47 (38%)—an unusually high proportion of paratyphoid cases infected from water.

The incidence in the sexes was equal; the proportion of child patients under 10 years was increased in comparison with preceding years; the decline in the number of paratyphoid cases was greater than in the typhoid cases; small outbreaks in villages and small towns were more frequent. The percentage of patients who had had TAB inoculations was less than in preceding years, and the number of such vaccinations given more than 10 years before the illness was greater than it was formerly. The prognosis seemed to be influenced only by the age factor, and not by the kind of organism, the source of contamination, or prophylactic inoculations; the latter, however, were practically confined to adults, in whom the disease is usually more serious than in children. The case fatality rate, calculated only on the number of patients whose illness was officially observed, was 2·4%, and was similar to that of the preceding years.

H. Stanley Banks

PILSWORTH, R. **Detection of a Carrier of *Salm. typhi* by means of Sewer Swabs.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1960, Nov., v. 19, 201–7, 1 fig.

This is a further example of the value of the sewer swab method [this *Bulletin*, 1949, v. 24, 187] for the detection of a carrier in the investigation of an outbreak of typhoid fever which involved comparatively few persons but continued for a number of years. When the investigation eventually pinpointed a particular house it was found that one of the occupants had suffered from typhoid fever several years previously and was excreting typhoid bacilli of the same phage type as that causing the outbreak. The chain of epidemiological evidence was somewhat complicated in the outbreak and was not complete.

Some interesting observations were made in the bacteriological work involved. Brilliant green selenite broth containing sulphonamide was found superior to the usual selenite F enrichment medium. Incubation of the inoculated enrichment medium at 43°C. which HARVEY and THOMSON [*ibid.*, 1954, v. 29, 97] had found was better than 37°C. in the case of *Salmonella paratyphi B* infections did not prove to be satisfactory in the present investigation.

H. J. Bensted

DEL NEGRO, G. Consideracões clínicas sôbre a febre tifóide na criança. Análise de 60 casos. **[Clinical Aspects of Typhoid Fever in Children; Analysis of 60 Cases]** Reprinted from *Rev. Hosp. Clín.* 1960, Nov.–Dec., v. 15, No. 6, 394–404. [10 refs.] English summary.

This is a study of typhoid fever as it occurred in 60 children less than 15 years old who were in-patients at the University of São Paulo Hospital between 1952 and 1959. In 6 the diagnosis was purely clinical. 48 were

over 7 years of age, 35 were boys, most came from the outskirts of the city. The average duration of the illness before admission was 13 days.

The onset was *sudden* in 30 and gradual in 24, fever was by far the most common symptom with headache, anorexia, asthenia, prostration, and somnolence next in descending order. In 70% there was no change in mental alertness. 26 had initial diarrhoea, 18 " bronchitis ", and 70% splenic and liver enlargement. No dissociation between pulse and temperature was found. Blood cultures were made in 56 of the 60 cases, 19 were positive; bone marrow cultures in 15 gave 8 positive, 4 of whom were negative to blood culture. Urine culture in 30 was negative. *Salm. typhi* was isolated from the bile in 1 case out 9. In 4 patients *Shigella* species were also isolated, and in 1 *Salm. enteritidis*.

The Widal test was performed on 58 of the 60. In 3 it was always negative though both blood and marrow cultures were positive; 4 others had H always negative but 0 more than 1:60. In 51 out of 58 the sera were definitely positive. About 50% had no leucopenia but although the majority had an intestinal helminth infection as well, 80% showed a *fall* in the eosinophils, rises only occurring in those with schistosomiasis.

Complications arose in several patients. Perforation occurred in 7, 3 of whom died. Typhoid septicaemia was present in 2, 1 fatal; and peritonitis, appendicitis, and intestinal haemorrhage in 1 each, all of whom recovered. In all 56 patients were cured, 2 of whom had a previous relapse.

55 of the 60 were treated with chloramphenicol (average dose 50 mgm. per kgm. body-weight); 3 were cured without this drug. The average period until the patients became afebrile under chloramphenicol was 5–6 days (the author states that the unusual length may have been due to the inferior quality of the drug). 1 patient who did not respond became afebrile in 24 hours after prednisone. *W. K. Dunscombe*

Pianese, G. & Raimondi, A. Comportamento delle prove allergiche e delle sieroagglutinazioni, in ex-brucellotici, a distanza varia dalla malattia. [**The Behaviour of Intradermal and Agglutination Tests in Persons Recovered from Brucellosis, Some Years after the Disease**] *Nuovi Ann. d'Igiene e Microbiol.* 1960, Sept.–Oct., v. 11, No. 5, 420–34. [21 refs.]

The authors point out that it is now known that, like tuberculosis, brucellosis causes a definite allergic state in most of those affected, usually beginning in the first few weeks of the disease, increasing in intensity as the disease progresses, and lasting for years. Their report covers tests on 195 patients near Naples who had had brucellosis 1–8 years previously. 105 of these lived in a zone of high endemicity (area A) and the remainder in a low endemic zone (B). This choice was made deliberately to see if continuous or repeated contact with *Brucella* antigen had any effect.

On each patient agglutination tests were carried out before, and 14 days after an intradermal (ID) test with an antigen made up of the soluble and insoluble products of 100×10^6 *Br. melitensis*, 0·1 ml. being injected into the forearm and read after 48 hours; those showing oedema, heat, and redness persisting for 3–4 days were considered positive. The serum tests were performed against all 3 *Brucella* types, and sera were heated to 56–58°C. to attenuate or destroy coagglutinins. The patients in the 2 groups were fairly comparable as regards the length of time since the disease ended.

The results were: of the 105 in area A 66 showed antibodies 12 of whom had a titre of 1:30 or more 4 years after infection, while 6 had titres of 1:30 6 years after, and 3 1:20 or 1:30 8 years after. In area B 49 were negative, and of the 41 positive 2 had titres of 1:30 or more 4 years after, and 2 had 1:20 7 years after infection. However in the first few years after infection there appeared to be little difference between the 2 groups and this became more marked after the 4th year. In the ID tests in area A, 34 were negative, and 42 were negative in area B. Aggultination tests 14 days after the ID test showed 32 negative in area A but in all the positives the titre was considerably raised compared with that before the ID test; in area B, 43 were negative but here again the titres were considerably higher in those positive. In both the titres increased only in those sensitive to the ID test.

The authors conclude: (1) massive and repeated contact with the organism is of great importance in maintaining allergy and also positive agglutinin titres; (2) allergy usually persists longer than agglutinins; (3) in those ID positive but sero-negative, contact with a *Brucella* antigen gives rise to circulating antibodies; (4) the appearance of, or increase in, agglutinin titres after ID tests only occurs in those showing hypersensitivity to the ID test.

[If these results can be confirmed elsewhere they may be of material assistance in the diagnosis of those very difficult " rheumatism-like " illnesses with a low *Brucella* agglutinin titre.] *W. K. Dunscombe*

Pavlov, P., Dimov, D., Tchilev, D. & Janev, J. Présence dans le sérum de la tortue *Testudo graeca* en Bulgarie d'anticorps agglutinant *Pasteurella tularensis*. [**Examination in Bulgaria of *Testudo graeca* for the Presence of Antibodies agglutinating *Brucella tularensis***] *Ann. Inst. Pasteur.* 1961, Feb., v. 100, No. 2, 261–3.

The English summary appended to the paper is as follows:—

" 26 p. 100 of the sera of *Testudo graeca* captured in Bulgaria agglutinate *P. tularensis* at high titers (1/100 to 1/3 200). This frequency and high titers contrast with the absence of agglutinins in human beings, foxes, hares, etc.

" No strains of *P. tularensis* have been thus far isolated in Bulgaria, even from tortoises yielding positive serological reactions and from their ticks.

" Further studies are in progress."

Patel, J. C., Dhirawani, M. K., Mehta, B. C. & Agarwal, K. K. **Tetanus following Intramuscular Injection.** *J. Indian Med. Ass.* 1960, Dec. 1, v. 35, No. 11, 505–7.

In a 4-year period 2,007 cases of tetanus were treated in the King Edward Memorial Hospital, Bombay: in 32,

the organism appeared to have been introduced during the intramuscular injection of a drug. 27 of the 32 patients died; the mortality being 84·4% as compared with the mortality of all the cases of 43·7%. Faulty technique was of course the cause but the authors felt that necrosis of tissue due to the injected drug facilitated growth of the organism. *A. B. Christie*

LESSARD, R., POTVIN, A. & MORIN, Y. L'emploi du méthocarbamol dans le tétanos: abord expérimentale et clinique. **[The Use of Methocarbamol in Tetanus: Experimental and Clinical Study]** *Canadian Med. Ass. J.* 1960, Dec. 3, v. 83, No. 23, 1199–202, 6 figs.

Methocarbamol was given intravenously to 2 patients suffering from tetanus. Both recovered, 1 after a very severe attack which developed 5 days after criminal abortion. The drug was given intravenously up to 16 gm. per day: it controls major convulsions without interfering with spontaneous respiration. In rabbits it appears to be surer and more efficacious than curare. Antibiotics, antitoxin and tracheotomy are required as well.

A. B. Christie

BUSHILA, V. T. & PON, O. **Questions of the Pathogenesis and Treatment of Tetanus of the Newborn.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1960, v. 31, No. 3, 503–8, 5 figs. [Translated from Russian.]

The authors studied pneumograms in babies suffering from tetanus and found evidence of increased excitability of the respiratory centre. They found that feeding with maternal milk through a small Nelaton's tube combined with the injection of luminal (phenobarbitone) led to alleviation of the condition for 3 to 4 hours. They claim a substantial reduction of mortality but no details of treatment are given. *A. B. Christie*

BOEREMA, I. & BRUMMELKAMP, W. H. Behandeling van anaërobe infecties met inademing van zuurstof onder een druk van drie atmosferen. **[Treatment of Anaerobic Infections by the Introduction of Pure Oxygen under a Pressure of Three Atmospheres]** *Nederl. Tijdschr. v. Geneesk.* 1960, Dec. 17, v. 104, No. 51, 2548–50. English summary (5 lines).

The authors have been using the inhalation of high pressure pure oxygen, with particular reference to surgery, for four years. This is a preliminary report of the encouraging results obtained in 3 hopeless cases of gas gangrene complicating surgery.

The first a woman of 26 (who had had a post-appendicectomy gangrene, and had responded to the usual treatment in 1956–57) developed an extensive gas gangrene of the lower abdomen following an oöphorectomy in August 1960. She had 5 2-hour daily sessions of the inhalation of pure oxygen at 3 atmospheric pressures. Within 24 hours there was a marked improvement and except for the original wound, recovery was uneventful. Bacteriology was negative.

The second, a man of 67 years, developed gas gangrene after amputation above the knee (because of arteriosclerotic gangrene of the foot). Initial treatment had been disarticulation at the hip, but the whole lower abdomen became involved and *Clostridium welchii* was isolated. Treatment comprised 3 sessions during the first 24 hours; after the second, improvement set in and the gaseous lesion was seen to be regressing. 7 sessions over 3 days resulted in cure of the gas gangrene and progress thereafter was satisfactory.

The third was a boy aged 13 in whom *Cl. welchii* invaded a complicated fracture of the forearm. Amputation of the arm had been unsuccessful and the patient became comatose and had convulsions. Treatment consisted of 2 hours of pure oxygen at 3 atmospheric pressures. After 6 hours the patient's condition was described as good. He had a total of 7 sessions over 4 days after which his progress was first class.

Only 3 proper high pressure chambers are available in the Netherlands, in Amsterdam, Den Helder and Vlissingen, but the authors welcome enquiries and offer any help they can in problems of this kind. *Kurt Schwarz*

MOCHMANN, H., LEOPOLD, P. G. & GRIEM, Rita. Zur Epidemiologie des Morbus Weil in einer Grossstadt. **[On the Epidemiology of Weil's Disease in a Large Town]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 4, 537–48, 2 figs.

Since 1949 the Rostock Leptospiral Laboratory in East Germany has recorded 326 cases of Weil's disease and there is a spot map of the whole area which shows their geographical distribution. Particular attention was focused on the city of Leipzig because of the occurrence in 1957 of an outbreak of 6 cases of the disease among the animal keepers in the zoo. The source of the causative organism was found to be wild rats from the zoo park which had been used in the feeding of young owls. 5 of 15 wild rats were shown to be leptospiral carriers and from 1 of these a virulent strain of *L. icterohaemorrhagiae* was isolated.

This small epidemic led to further investigations in Leipzig. Of 63 wild rats from the zoo, sewage works, slaughter-house and elsewhere 33 were found to be leptospiral carriers. Serological testing carried out in 1958–59 yielded positive results for leptospira of Weil's disease in 7 of the 46 zoo workers who had had the clinical infection previously and also in 10 of a group of 66 workers engaged in sewer cleaning. Tests in 74 other workers in the water and sewage works yielded only 2 positives. Some clinical particulars are given of those serologically positive persons in these 2 tested groups who are known to have had Weil's disease. It is noted that in others a Weil's infection may have been missed either because it was of abortive type or was misdiagnosed as influenza, epidemic hepatitis or other disease.

There is a table which gives some details of the 36

cases of Weil's disease which have definitely been diagnosed in Leipzig since 1935 and these are discussed from the epidemiological and clinical standpoints.

M. E. Delafield

FUCHS, G. H. P. Zur Problematik arbeitsbedingter Leptospiren-Infektionen bei Angehörigen sog. Schmutzberufe. [**The Problems of Occupational Leptospirosis in So-Called Dirty Professions**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 4, 549–61. [95 refs.]

To introduce the work reported in this paper there are references to the relevant literature which indicates not only the frequency of leptospiral infections in certain occupations but also the importance of laboratory testing for such infections in the investigation of febrile diseases in the general population since omission of such tests has frequently led to clinical mis-diagnosis.

In the work described sera from 487 persons—443 of whom were engaged in "dirty" work such as canal and sewage work, river work, dust and garbage carting and street cleaning, and 44 in mining—were examined by the agglutination-lysis test against 18 different leptospiral antigens.

The findings of the serum tests are described and discussed with the main conclusions that positive reactions to *L. icterohaemorrhagiae* were found in 14 (3·2%) of 443 from the "dirty" occupations with figures of 4·9% for sewage workers, 7·4% for garbage workers but only 0·9% in the street cleaners which is about the same as in the average population. Positive tests against *L. grippotyphosa* were obtained in sera from 7 of the 218 street cleaners, 1 of the 22 river workers and 2 of the 44 miners.

M. E. Delafield

FUZI, M. Eine Plattenmethode für die Agglutination-Lysis-Reaktion bei Leptospirose [**Plate Method for Observing Agglutination-Lysis of Leptospires**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1960, Nov., v. 120, No. 4, 199–206, 4 figs.

This paper deals entirely with the technique of determining agglutination-lysis of leptospires in laboratories in which a very large number of such examinations have to be made, as in the author's own where many thousands of sera are investigated annually and 30–40 different antigens are used. The methods are therefore adopted to save time at every point. A cupped plastic plate is used instead of tubes and a holder carrying 6 metal loops 3 mm. in diameter so disposed that they can be dipped into 6 cups simultaneously. Loopfuls of serum dilutions and antigen suspensions are rapidly mixed in this way and allowed to stand for one hour at room temperature. With the same multiple loopholder a series of drops are transferred to a microscope slide and these are observed under dark ground illumination. The limit of activitity of any serum is taken as the dilution in which there is observed a 25% loss of free mobile leptospires. *J. W. McLeod*

VIRUS INFECTIONS

The order in this section is:—***General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Reovirus group; Enteric group; Arthropod-borne group; Others.***

JANSSON, E. **Ornithosis in Helsinki and some other Localities in Finland. A Serological and Clinical Study.** *Ann. Med. Exper. et Biol. Fenniae.* Helsinki. 1960, v. 38, Suppl. 4, 110 pp., 13 figs. [137 refs.]

This monograph records the investigations made by the author to discover what part, if any, ornithosis virus was playing in Finland in the causation of atypical pneumonia and other respiratory infections. Helsinki provided the major part of the material for these researches which were made in the Municipal Bacteriologic Laboratory in the Aurora Hospital of that city. 758 patients with pneumonia —546 of them from Helsinki—and 236 cases of acute upper respiratory disease were investigated and of these 43 were found to have a significantly rising titre of psittacosis group antibody or a falling one from an initially high level. 18 of these 43, or 42%, were children aged 1 to 15 years; the oldest patient was aged 82. The sera from 16 of these 43 patients were examined with negative results for Q fever antibody. And although adenovirus antibodies, with titres of 1 in 8 to 1 in 64, were found in 19 serum pairs from 38 of these patients, in no cases did these antibodies undergo significant fluctuation.

The author concludes that these 43 patients were suffering from acute ornithosis and states that of the cases treated for pneumonia in the Aurora Hospital in Helsinki during the period of the investigation—October 1958 to May 1960 —5·6% were due to ornithosis virus, an incidence very similar to that which has been found in other countries. The 43 cases are described in some detail and among other points of interest which emerge from these accounts is the absence of evidence in many of them that the infection had come from birds. In 31 this was completely lacking and in the remaining 12 it was not always very convincing though the uniformity with which it pointed to pigeons as the source of trouble was suggestive.

In the hope of getting further evidence of an avian source of infection, the incidence of ornithosis antibody in groups of individuals with bird contact—cage bird owners (65), poultry farmers (72) and pigeon exterminators (12)—was compared with its presence in control groups; children undergoing surgical treatment (93), medical students (59) and blood donors (998) were chosen as controls. This survey was perhaps not very revealing. Cage birds were exonerated though poultry emerged suspect and 4 of the 12 men concerned with pigeon destruction had psittacosis-group antibody in their sera at quite substantial titre (1 in 20—1 in 80). It is admitted, of course, that the number of individuals in this last group is so small as to make it impossible to draw any firm conclusion, but here again evidence points to the pigeon as a source of infection. This led to an attempt directly to assess the extent of infection of the Helsinki pigeons with ornithosis virus.

To this end serum samples from 646 pigeons, caught in different parts of the city, were examined for the presence of ornithosis antibody by the direct complement-fixation

test and it was found in significant amount in 15 to 55%, according to the different parts of the city from which the birds came, an average of 28%. When sera from 95 pigeons caught in 8 different parts of the city were examined by both direct and indirect complement-fixation tests, 25% were positive by the former and 63% by the latter; 79% by the 2. As the author remarks: "Bearing in mind that the number of pigeons in this city of 400,000 inhabitants is estimated to be about 30,000, it is evident that pigeons are a considerable infective risk to the inhabitants." *S. P. Bedson*

AGARWAL, B. L. **Haemorrhagic Smallpox. (Purpura Variolosa.)** *J. Ass. Physicians India.* 1960, Nov., v. 8, No. 6, 577–82, 1 fig.

The importance of the distinction between purpura variolosa (toxic or haemorrhagic smallpox) and variola pustulosa haemorrhagica is not always sufficiently realized. The former type of the disease carries a mortality of 100%, and, especially in sporadic cases, the true diagnosis is likely to be missed and the patient admitted to a general hospital. In variola pustulosa haemorrhagica, where haemorrhages accompany or follow the focal eruption, the outlook is apt to be more favourable. Details are given here of 13 fatal cases of haemorrhagic smallpox which occurred during a period of 7 months in Kanpur.

In the present series the majority of the patients were admitted to hospital on the 3rd or 4th day of illness with fever and severe low backache. 7 pregnant women were suspected of threatened abortion: 4 others presented as cases of "acute abdomen". Except in 2 cases high fever was not a prominent feature, but all patients had haemorrhagic manifestations, of which sub-conjunctival haemorrhages and bleeding per vaginam and at injection sites were prominent early. Most patients were mentally confused and restless: the average duration of the disease was just over 5 days. With 2 exceptions the age of the patients ranged from 20 to 28 years. The exceptions were a male of 3 and a female of 40 years.

The vaccination state of each individual is not given: it is only recorded that "Except for two cases who could not give a proper history, all the cases were vaccinated in childhood. The marks of vaccination however were not evident in 3 cases". A leucocytosis of 15,000 to 27,000 per cmm. predominately lymphocytic (over 50% of the total count) was considered to be a characteristic finding.

J. Pickford Marsden

DEODHAR, N. S. & DONGRE, P. M. **Small Pox within Nine Months of Primary Vaccination. A Case Report.** *Indian Med. J.* 1960, Sept., v. 54, No. 9, 199–200, 3 figs. on pl.

WIELENGA, G., VAN TONGEREN, H. A. E., FERGUSON, A. H. & VAN RIJSSEL, T. G. **Prenatal Infection with Vaccinia Virus.** *Lancet.* 1961, Feb. 4, 258–60. [10 refs.]

A premature infant (27½ weeks) who lived for 10 minutes, was born with extensive skin lesions which were shown histologically and virologically to be vaccinial. Lesions were also present in other organs of the body and in the placenta.

The mother had never been vaccinated and bore no scars, but 8 days after delivery vaccinia-virus neutralizing antibodies at a high titre were present in her serum.

When her pregnancy had lasted 18 weeks her son aged 11 months was successfully vaccinated. About a week after this success had become apparent the mother developed a sore throat and fever for which she remained in bed for 10 days. The authors postulate that the illness at this time must have been the result of airborne infection with vaccinia virus.

[A strange, mysterious, story.] *J. P. Marsden*

ANTONOVA, N. I. **Virological and Serological Investigation of Acute Aphthous Stomatitis in Children.** *Acta Virologica.* Prague. 1960, Nov., v. 4, No. 6, 383–91, 3 figs. on pl. [19 refs.]

Herpes simplex virus was isolated from 14 out of 16 children with acute aphthous stomatitis by inoculating mice intracerebrally with scrapings from the lesions. The 2 failures are explained by the fact that isolation was not attempted until 7 days after the onset of the disease in these cases. Virus was also isolated in human embryo tissue culture from 8 of the children. It produced a cytopathic effect resembling that caused by herpes growing in HeLa or human amnion cells. The virus was identified by neutralization tests. *Janice Taverne*

BOHANES, M., GROMBÍR, J., GRÜNNER, O., KNOZ, J., STRNAD, A. & VALIHRACH, J. Ornitózové neuroinfekce. **[Ornithosis Neuroinfections]** *Časopis Lékařů Českých.* Prague. 1960, Sept. 23, v. 99, No. 39, 1238–42. [12 refs.] English summary.

Between 1956 and 1958 the authors have observed 11 cases of involvement of the central nervous system in patients suffering from confirmed or probable ornithosis; 2 cases are to be published elsewhere and histories of the remaining 9 are presented. The patients were all admitted to the authors' hospital in Czechoslovakia; 5 were suffering from encephalitis and 3 from peripheral involvement of the nervous system (polyradiculitis, facial neuritis). Convalescence was protracted and accompanied by a neurotic state. Two patients showed haemorrhagic manifestations (exanthem, haemorrhagic retinitis). In most cases the illness had taken a biphasic course. Contact with sick poultry could be established, and in 1 case a dead seagull may have been the source of infection. The diagnosis was confirmed by virological methods in 5 cases.

D. J. Bauer

RINGLEBEN, H. Verwildert Haustauben in hygienischer Sicht. **[The Pigeon Nuisance in Cities]** *Desinfektion u. Gesundheitswesen.* 1960, Sept., v. 52, No. 9, 124–8, 4 figs. [11 refs.]

This is an interesting account with some photographs of the pigeon nuisance and of the extent to which pigeons have multiplied in a number of German cities. The increase is considered to be due largely to there having been so many suitable nesting places resulting from the

bombing of cities during the war and also to the eagerness of the inhabitants to feed these birds. Many domestic pigeons (Haustaben) which at one time were kept in pigeon-lofts and flew to the country for food have availed themselves of the amenities of the city and have gone to a wild and freer life.

Some information is given on populations of pigeons in different cities, for example in Hamburg where the estimate is between 15,000 and 20,000 birds. Investigation has shown that the average annual weight of excreta per bird is 2¼ to 2¾ kgm.

Although these birds are a pleasure for many there are drawbacks to their presence among which are mentioned the disfigurement of buildings and statues, the evil odour of the excreta, slippery pavements and the actual damage to buildings due to pecking of the birds at the mortar because the food given them is lacking in calcium and grit.

There are also positive hygienic dangers which are described. A list is given of the large number of vermin found in the nests and excreta which includes mites, fleas, larvae of moths, beetles, larvae of flies, ticks and bugs. Mention is made of the possible danger of spread of bacterial infection such as salmonellosis by pigeons. The paper ends with a considerable description and discussion of ornithosis and its possible transmission to man. A considerable percentage of pigeons have been shown to be virus carriers and in Hamburg 9·8% of the birds were found to be carrying the pigeon virus. In Germany only 30 human cases of ornithosis have been diagnosed with certainty but this number is likely to represent only a small percentage of the actual number of infections.

M. E. Delafield.

Povolotskii, I. L. **Serological Investigations in the Epidemic Parotitis.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 10, 144–51. [Translated from Russian.]

In an investigation of 211 sera obtained from patients with mumps at various times up to 1 year from the onset of illness it was found that the titre of haemagglutination-inhibition reached a maximum of 80 or higher after 2-4 weeks and remained at a fairly high level for 3-6 months.

Complement-fixing antibody appeared sooner than inhibiting antibody, but otherwise behaved similarly. In the examination of 127 sera from blood donors titres of inhibiting and complement-fixing antibody of 20-40 were found in 41 (32·3%) and 36 (28·3%) instances, and of 80 or higher in 2 instances each (1·6%). Among 56 children who were exposed to mumps without contracting the disease a 4-fold or greater rise in titre in paired sera taken at the beginning and end of the period of exposure was found in 11 (19%) by the haemagglutination-inhibition and in 13 (23%) by the complement-fixation test. The rise in titre was considered to indicate the occurrence of asymptomatic infection.

D. J. Bauer

Hamre, Dorothy, Lashof, Joyce C., Marshall, J. A., Cassidy, J. E., Smith, Mabel & Bennett, C. R. **A Study of Viruses implicated in Acute Respiratory Disease in Chicago from October, 1958, to June, 1959.** *Amer. Rev. Respiratory Dis.* 1961, Jan., v. 83, No. 1, 38–42. [14 refs.]

"Two hundred and thirty-seven patients with respiratory disease were studied in an effort to make an etiologic diagnosis. In only 43 cases were known viruses implicated. Influenza A and B accounted for 29 illnesses, or 12% of the total. Adenovirus, para-influenza 1 and 2, and chimpanzee coryza agent appeared to be related to illness in 14 cases, or 6% of the total. The etiology of the vast majority of respiratory disease remains undefined."

Leonardi, G., Moro, V. & Zulian, G. Terapia e profilassi dell'influenza con xenalamina, chemioterapico antivirale di sintesi. [**The Curative and Prophylactic Treatment of Influenza with Xenalamine, a Synthetic Antiviral Drug**] *Giorn. di Malattie Infettive e Parassit.* 1960, Aug., v. 12, No. 8, 419–25, 8 figs.

The formula of xenalamine is given as p-(α-ethoxy-p-diphenylacylamine) benzoic acid. The authors administered the drug to 53 patients with influenza due to the A-Asian virus, while 47 other patients in the same outbreak were given pyramidone and vitamin C and were observed as controls. The dosage of the xenalamine was 25 mgm. per kgm. of body weight daily in children, and 1·5 gm. as a total dose daily for adults, in a course of 4-5 days. The virus was recovered from pharyngeal washings which were taken before treatment; another specimen was examined 96 hours later. Nearly all 53 patients were apyretic within 48, 30 within 24, hours of commencing treatment. In the 47 control patients pyramidone with vitamin C took 48-72 hours to achieve defervescence. The course of other signs and symptoms in the 2 groups showed significant differences in favour of the new drug.

The authors have also studied 134 contacts of these patients distributed in 25 households. As a prophylactic measure, they gave 42 of these contacts a 5-days' course of the new drug—1 gm. daily to adults and 25 mgm. per kgm. body weight to children—and 3 of these (7·1%) contracted the illness, which affected 37 of the 92 (40·2%) contacts who had not received the course of prophylactic treatment.

An interval of 12–36 hours elapsed between onset of illness and commencement of treatment in this series; more striking benefits may be gained if xenalamine could be started at an earlier stage of the illness. *J. Cauchi*

Pattyn, S. R. & Delville, J. P., with the technical collaboration of J. Peel & A. Gantois. Contribution à l'étude des adénovirus à Elisabethville. [**Adenovirus Infections in Elisabethville**] *Ann. Soc. Belge de Méd. Trop.* 1960, Apr. 30, v. 40, No. 2, 373–87, 1 graph. [11 refs.]

Between May 1957 and February 1959, 1,454 faecal specimens were collected from Congolese children with minor ailments who attended the Prince Léopold Hospital, Elisabethville, and also from a few school children. The ages of the children ranged from a few months to 6 years.

Adenoviruses were isolated from 3% of the specimens; thus, 44 strains were isolated in HeLa and secondary human amnion cultures, the latter being more sensitive. Neutralization with type-specific rabbit sera revealed the

following types in decreasing order of frequency: 6, 3, 2, 12, 16, 5, 8. There were 12 isolations of type 6 adenovirus and 11 of type 3.

Cord, infant and adult sera were used in neutralization tests against adenovirus types 1, 2, 3, 5, 6, 7, 10 and 12. Antibodies were frequently found against those virus types that had been isolated (2, 3, 5, 6 and 12) but very infrequently against types 7 and 10 that were not isolated. However, antibodies to type 1 virus were found in 56% of all the sera tested, although this virus had not been isolated; the authors suggest that this virus type might be transmitted *via* the respiratory tract. A further interesting feature was the isolation of 4 strains of type 12 virus and the presence of antibodies in 76% of adult sera tested; this virus type is usually rare. In general, the antibody pattern for the various virus types was similar to that for poliomyelitis in the Congo; antibodies were frequent in cord blood, diminished in the first 2–4 years of life and increased thereafter. *D. Taylor-Robinson*

FERRIS, A. A. **The Croup Viruses: Bacteriological Aspects.** *Med. J. Australia.* 1960, Nov. 12, v. 2, No. 20, 768–9.

Throat swabs were collected from all of 227 patients admitted to Fairfield Hospital, Melbourne, Australia, and suffering from croup. The swabs were tested for the presence of para-influenza viruses. Between May 1959 and March 1960 inclusive 72 viruses were isolated from these patients and only 9 from 1,369 patients suffering from other diseases apparently including a minority of others (children and adults) who suffered from minor respiratory illness. 52 viruses were type I (HA2) and were isolated towards the end of the study; the remainder were type III (HA1) and isolated towards the beginning of the study. In the last 3 months the type I virus was isolated from 46 of 83 patients tested. *D. A. J. Tyrrell*

FORBES, J. A. **Croup Viruses: Clinical Aspects.** *Med. J. Australia.* 1960, Nov. 12, v. 2, No. 20, 769–71, 1 fig.

A short account is given of clinical observation on the patients from whom para-influenza viruses were isolated [see FERRIS, above]. 70% of patients were under 5 years of age. The illness often began with coryza followed by laryngo-tracheo-bronchitis (LTB) in 1 to 3 days or occasionally less. A few patients were suffering from non-specific fever during convalescence from another illness and a few from pneumonia. Adult relatives of the patients gave a history of colds but only rarely were adults with severe disease, such as croup, seen. There was a relatively higher proportion of pneumonia to LTB in patients from whom influenza A2 virus was isolated. The author considers that diagnosis on clinical grounds is uncertain but a normal or low blood leucocyte count with a preponderance of lymphocytes may suggest a virus infection. He advocates treatment "with antibiotics as if bacterial infection was already established."

D. A. J. Tyrrell

CRAIGHEAD, J. E., SHELOKOV, A., PERALTA, Pauline H. & VOGEL, J. E. **Croup-Associated Virus Infection in Adults. Report of Two Cases.** *New England J. of Med.* 1961, Jan. 19, v. 264, No. 3, 135–7. [10 refs.]

"Infections with croup-associated (parainfluenza 2) virus were demonstrated in 2 young adults with febrile systemic illnesses of short duration. Evidence of infection was based on recovery of the virus at the time of acute symptoms and antibody rises during convalescence. These findings suggest that croup-associated virus was responsible for the illness of both patients."

SUREAU, P., with the technical collaboration of RAZAFIMAHATRATRA & R. RABESOA. Bilan de dix-huit mois de recherche des entero-virus à Madagascar. **[Results of 18 Months' Study of Enteroviruses in Madagascar]** *Arch. Inst. Pasteur de Madagascar.* 1960, v. 28, 97–107.

In the period August 1958 to December 31, 1959, 40 enteroviruses were isolated in KB cells or suckling mice from sick children (usually with poliomyelitis) or their contacts in Madagascar. In all, 36 persons yielded a virus. 26 excreted poliovirus: 16 type 1, 9 type 2 and 1 type 3. The Coxsackie viruses were all group A but have not as yet been classified. 2 patients who had paralytic poliomyelitis yielded a Coxsackie A virus but no poliovirus.

A. J. Beale

DAVIES, A. M., MARBERG, K., GOLDBLUM, N., LEVINE, Sonia & YEKUTIEL, P. **Epidemiology of Poliomyelitis in Israel, 1952–59, with Evaluation of Salk Vaccination during a Three-Year Period.** *Bull. World Health Organization.* Geneva. 1960, v. 23, No. 1, 53–72, 8 figs. [30 refs.]

This long paper investigates the effectiveness of poliovaccine in Israel against the broad background of the epidemiology of the disease in the country. The first epidemic occurred in 1949 and since then until 1957 the rate has been 2.3 per 10,000 or more. The disease was infantile paralysis, 85–90% of the patients being under 5 years and 80% under 3 years. In 1957 a mass campaign of Salk vaccination was instituted and 89% of those between 6 months and 3 years had the first dose and virtually all had a second dose. The response in older children (3–3¾ years) was less good, 50–60% being vaccinated. The vaccination programme was less successful in country areas and in non-Jews than in Jews in urban areas. Because of shortage of vaccine, 0·3 ml. of vaccine was given in divided intradermal doses. Later, 0·5 ml. doses were given subcutaneously and, as vaccine became more plentiful, the dose was increased to 1 ml. Moreover, as vaccine became more plentiful, it also increased in potency by 10–30 fold as judged by antigen extinction titres in guineapigs. Before 1955 it appears that poliomyelitis virus type 1 was probably the most prevalent type. In 1957, which was not an epidemic year, 36 poliomyelitis viruses were isolated—4 type 1, 19 type 2 and 13 type 3—but in the epidemic of 1958 type 1 predominated although, especially among the non-vaccinated and

non-Jewish population, many type 2 and 3 strains were isolated. In 1959 type 1 isolations were again scarce. Serological studies confirmed the data derived from the age incidence of poliomyelitis by showing the rapid acquisition of antibodies. Thus, in the 1958 outbreak, the protective effect of being 4 years as opposed to 1 year was 88%.

In 1958 there was an extensive outbreak with an attack rate of 3 per 10,000 for Jews and 2 for non-Jews. The patients were mainly under 3 years of age. The rise in incidence of poliomyelitis was found to run parallel with the loss of antibodies to poliovirus in the first 6 months of life. The mortality during the 1959 epidemic was 9·2%. In analysing the effectiveness of vaccine, attention was confined to 2 areas, Jerusalem and Ashkelon, and to a narrow age band (those born in 1957, *i.e.* 6-18 months at the time of the epidemic) because of variations in incidence with age and location and difficulties in obtaining demographic data. The districts analysed had very high attack rates, but the monthly attack rate per 10,000 was 59 in those who had received 0–1 doses and 25 in those who had had 2 doses, giving an effectiveness of 58%. There were no cases in those given 3 doses. In 1959 there were too few cases for statistical analysis. Between 6 months and 2 years there were 21 cases and 1 death in a population 76% of whom had had 2 or more doses of vaccine. 12 of the patients, including the fatal case, had had no or only 1 dose of vaccine, implying high effectiveness.

[This is an interesting paper illustrating the complexities of poliovirus epidemiology and the difficulties of assessing the effectiveness of preventive measures.] *A. J. Beale*

Leonardi, G., Gasparini, V., Ghio, T., Moro, V. & Zulian, G. Studio di un focolaio epidemico di poliomielite. Profilassi vaccinica e gamma-globulinica dei "contatti". **[Study of an Epidemic Focus of Poliomyelitis. Prophylactic Vaccination and Administration of Gamma-globulin to Contacts]** *Giorn. di Malattie Infettive e Parassit.* 1960, Aug., v. 12, No. 8, 431–6, 3 figs.

Between April 5 and 11, 1959, 5 children with acute anterior poliomyelitis were admitted into hospital at Portogruaro, in the Trieste area. The epidemiological enquiries established contact links in every case: 4 lived in the same street of an outlying suburb, where was an infant institute which 3 attended. There were 45 other children at this place and one of these was taken away by the parents when the outbreak occurred. None had been vaccinated against poliomyelitis. The stools of the 44 contacts were examined and 5 were found to be symptomless excreters of type 1 virus. Blood specimens were taken on April 24 and again a fortnight after that, when 7 showed that there had been a rise in antibody titre to type 1 virus, one of the symptomless excreters being among these. On the outbreak appearing, 22 of the contacts were given a first dose of Salk vaccine and 3 of these were among the 7 who showed a rise in immune titre.

For passive immunization, the 44 contacts were given each 0·2 c.c. of gamma globulin per kgm. of body weight, and this is believed to have helped in controlling the outbreak. Other preventive measures were taken—isolation of the patients, closure of the institution and quarantine of the staff.

The authors draw attention to their having given first injections of Salk vaccine to half the contacts after the outbreak had set in, without any unfavourable consequences. *J. Cauchi*

Salvaggio, L., Albano, A. & Bizzi, G. Comportamento degli anticorpi neutralizzanti antipoliomielitici di origine materna nel lattante. **[Behaviour in Infants of Poliomyelitis Neutralizing Antibodies of Maternal Origin]** *Riv. Istituto Sieroterap. Ital.* 1960, Nov.–Dec., v. 35, No. 6, 605–12, 1 fig. [23 refs.]

The English summary appended to the paper is as follows :—

"Investigations were carried out on the frequency, titer and persistence of poliovirus neutralizing antibodies (n.a.) of maternal origin in 28 infants.

"Type 1 and 2 n.a. are present in 100% of the children of 1 month of age, type 3 in 70%. Triple negative children were found from 3 months of age (23%); the percentage is increasing with age, reaching 83% at 7-8 months.

"N.a. titers above 1 : 64 were found in infants 1 month old to 3 months old for types 1 and 2, and 1 to 2 months old for type 3.

"The half life, i.e. the time in which the titer of n. a. is reduced to a half, was of 29 days for type 1 and 27 days for types 2 and 3."

Verlinde, J. D. & Wilterdink, J. B. De perorale vaccinatie tegen poliomyelitis. **[Peroral Vaccination against Poliomyelitis]** *Nederl. Tijdschr. v. Geneesk.* 1961, Jan. 7, v. 105, No. 1, 14–22, 8 figs. English summary.

This is a presentation of a report to the first (1959) and second (1960) International Conference on Living Poliovirus Vaccines, of results from the Netherlands during the period spring 1957 to autumn 1959.

225 individuals ranging in age from 7 weeks to 55 years received $10^{5,4}$ cytopathogenic doses of the 3 types of Sabin's live attenuated poliovirus. They were administered separately 0.1 ml. on a teaspoon of cream, in the order type 1, 3, 2 separated by intervals of 3 to 4 weeks.

(a) Prevaccination antibody titres related to age and type distribution are presented. 2 children in the series had received Salk vaccine. (b) Virus excretion studies showed 83 to 96% positive in non-immune children, maximal during the first 2 or 3 weeks followed by a sudden reduction. Individuals in the younger age-groups and those with homotype immunity were found to excrete less virus. (c) All non-immune children who excreted virus developed homotype antibodies. Similar findings were present in nearly all adults and non-excreters as well. Antibody levels fell in 15–22 months, but revaccination still showed reduced virus excretion, it being suggested that the local cellular reaction resembling natural infection is independent of the humoral response. (d) Neurovirulence was tested and type 3 showed a slight increase especially during the second to the fourth week.

During the period under investigation the general incidence of poliomyelitis was low. 5 designated areas were investigated virologically for poliomyelitis and enteroviruses (Coxsackie and ECHO) and the area (Leiden and environs) where the vaccination was carried out, showed in comparison no increased incidence.

Other workers' experiences are discussed with particular reference to increased post-excretion virulence, also the role of enterovirus infections interfering with the vaccine and thus preventing an antibody response. [See also this *Bulletin*, 1959, v. 34, 1088.] *Kurt Schwarz*

De Sanctis-Monaldi, T., Lippi, M., Sebastiani, A. & Frugoni, G. Esperimento di vaccinazione anti-poliomielitica con vaccino trivalente orale a virus attenuati di Cox [**Experiments with Cox's Oral Trivalent Anti-Polio Vaccine**] *Arch. Ital. Sci. Med. Trop. e Parassit.* 1960, Oct., v. 41, No. 10, 523–44. [71 refs.] English summary (5 lines).

According to the authors this is a live attenuated vaccine made up of type I (Mahoney); type II (MEF 1) and type III (Fox) and in testing it they aimed at studying: (1) its innocuity by clinical examination of the subjects; (2) titration of antibodies before and after vaccination.

The subjects were divided into 2 groups: (A) 16 adult volunteers, aged between 24 and 60 years; (B) 80 children from 13 months to 12 years of age in a convalescent home who were recovering from osteo-arthritic forms of tuberculosis, "lymphatism" or rickets. None of the adults had been vaccinated previously but all the children had had either 2 or 3 injections of Salk vaccine, the last of which was not less than 5 months previously.

All the subjects were given orally in 1 dose, 2 ml. of a viral suspension containing $10^{6 \cdot 1}$ $TCID_{50}$ of each type, the adults being vaccinated first, the children 1 month later. The following laboratory tests were carried out: (1) search for cytopathogenic viruses in the faeces before and 22–25 days after vaccination; (2) titration of antibodies before, and at 22–25, 40, and 60 days after in 25 children; (3) examination of faeces for viruses of 5 nurses (unvaccinated) attending the children in the home. The viruses used for titration of the sera were Mahoney, MEF 1, and Saukett.

Results. Before vaccination a type I virus was isolated from the faeces of a child admitted less than 48 hours before the test started (who was considered to have had a natural infection). None of the vaccinated persons had virus in the faeces 22–25 days after, but on the 15th day 1 of the nurses had a type III, and hence was definitely considered to have been infected. The findings in the 25 children are shown in tables but can be summarized as follows: Before vaccination the titre was $\geqslant 16$ in 14 for type I, in 11 for type II, and in 14 for type III; after vaccination this titre was reached by 23 for type I, 22 for type II, and for all 25 for type III. 10 of the 25 showed a 4-fold rise for all 3 types. Of 7 negative ($<1:4$) for type I before all showed some rise (but 1 only to 1:4); of 10 negative to type II, 2 showed no rise; in 9 negative for type III, the lowest titre after was 1:16, while of 6 triple negative subjects 3 were poor reactors for types I and II. The child from whom the type I was isolated before vaccination showed no rise at all, and in general those with a high initial homotypic titre showed a less response. No undesirable effects were found after repeated clinical examinations for a period of 2 months.

The authors conclude: (1) that the innocuity of the vaccine had been demonstrated; (2) types III and I showed a greater antigenicity than type II; (3) in 1 case a contact was infected; (4) the relative lack of success can be attributed to some immunity of the intestinal mucosa presumably due to some natural infection and not to the Salk vaccine.

[It is not at all clear, to the reviewer at least, why and how only 25 children were selected for antibody titration. The infection of the contact is certainly worthy of note.] *W. K. Dunscombe*

Walker, S. J., McLean, D. M., Roy, T. E., McNaughton, G. A. & Tibbles, J. A. R. **Infantile Gastroenteritis: A Search for Viral Pathogens.** *Canadian Med. Ass. J.* 1960, Dec. 10, v. 83, No. 24, 1266–7.

At the Hospital for Sick Children in Toronto efforts were made to isolate viruses from stools of patients with diarrhoea during 5 outbreaks of gastroenteritis during 1959 and 1960. 208 stool samples were obtained from children with gastroenteritis, mainly under 1 year old. These were all examined in monkey kidney cells. In addition, 131 were also examined in human amnion and 30 in suckling mice by the intracerebral route. No viruses were isolated and only 4% yielded a bacterial pathogen. During 1959 and 1960, 420 stool specimens were obtained from 349 children under 2 years old who were in hospital, but not suffering from gastroenteritis. 27 enteroviruses were isolated from 25 of these patients. *A. J. Beale*

Gold, E., Carver, D. H., Heineberg, Hannelore, Adelson, L. & Robbins, F. C. **Viral Infection: a Possible Cause of Sudden, Unexpected Death in Infants.** *New England J. of Med.* 1961, Jan. 12, v. 264, No. 2, 53–60, 2 figs. [16 refs.]

An attempt was made to isolate viral agents from 48 infants aged between 10 days and 2 years who died suddenly in Cuyahoga County, Cleveland, Ohio, between April and November 1957. In all cases, although a pathological diagnosis was made at autopsy, the anatomical findings were not considered adequate explanations for death. From 12 of the 48 infants, a virus was isolated, 5 from the gastro-intestinal tract and 7 from the central nervous system. The techniques used favoured the isolation of enteroviruses. From the faeces Coxsackie virus Group A type 8 was isolated twice, type 4 once, poliovirus type 3 once and an ECHO virus once: from brain suspensions, Coxsackie virus group A type 4 was isolated 6 times and poliovirus type 3 along with Coxsackie virus group A type 4 once. There were no morphological changes in the brain. [This is a very full discussion of the problem of sudden death in infancy; it should be carefully studied.] *A. B. Christie*

JUNNARKAR, R. V., SHARMA, K. D. & BERRY, J. N. **Autopsy Findings in Acute "Encephalitis" in Nagpur. Report of Five Cases.** *Indian J. Med. Sci.* 1960, Dec., v. 14, No. 12, 949–54, 7 figs. on 2 pls. [14 refs.]

Necropsies were obtained on 5 children who died in the encephalitis epidemic of 1958 in Nagpur [MUKHERJI *et al.*, this *Bulletin,* 1959, v. 34, 421; Berry *et al.,* 1960, v. 35, 61 *bis*]. Clinical details are scanty, since the children arrived at hospital in coma, and died within a few hours.

Necropsy findings were fairly uniform: the liver was fatty, the myocardium flabby with sparse round-cell infiltration, and the lungs intensely congested, with haemorrhagic exudate in the alveoli and petechiae beneath the pleura. In the brain, hyperaemia, oedema, and neuronal death were all unaccompanied by any notable glial or perivascular reaction; but there was an acute lymphocytic meningitis. In 2 instances an unsuccessful attempt was made to isolate a virus. However, the authors favour Coxsackie B virus as the infective agent, since the general pattern of organ involvement favours an enterovirus, and the observed nervous tissue lesions correspond more closely with Coxsackie than with ECHO or poliovirus infection. *Alan B. Raper*

VERETA, L. A. & SUSHKINA, L. M. **Some Results of Study of the Infection of *Ixodes* Ticks with Encephalitis Virus in Southern Districts of the Khabarovsk Region.** *Problems of Virology.* London, 1960, v. 5, No. 3, 319–24, 2 figs. [Translated from Russian.]

"(1) Two years' observations have established the high degree of infection with tick-borne encephalitis virus of the ticks *I. persulcatus* and *H. concinna.*

"(2) For the first time a strain was isolated from the tick *H. japonica douglasi* collected in the taiga. Apparently, *H. japonica douglasi* may also be the vector of tick-borne encephalitis in foci of the Khabarovsk region."

DOHERTY, R. L. & CARLEY, J. G. **Studies of Arthropod-Borne Virus Infections in Queensland. II. Serological Investigations of Antibodies to Dengue and Murray Valley Encephalitis in Eastern Queensland.** *Australian J. Exper. Biol. & Med. Sci.* 1960, Oct., v. 38, Pt. 5, 427–39. [29 refs.]

Sera from 70 patients clinically diagnosed as having dengue in an epidemic in 1954–5 [*Trop. Dis. Bull.,* 1957, v. 54, 1312] were tested for neutralizing antibody to dengue–1, dengue–2 and Murray Valley encephalitis (MVE) virus and for haemagglutinin-inhibiting (HI) antibody to MVE. The diagnosis was confirmed in 52 patients. Paired sera from 206 febrile patients from Innisfail between 1952 and 1955 were tested for MVE HI antibody: 10 had rising titres which neutralization tests showed were due to dengue. Of these 62 patients 31 had titres of 20 or more MVE complement-fixing (CF) antibody in convalescence, and these also showed rapid increases in MVE HI antibody. Most of them had dengue–2 neutralizing antibody in their 1st serum specimen. 25 patients developed MVE CF titres of 10 or less and much lower MVE HI responses. No acute phase serum in this group had dengue–2 neutralizing antibody and only 1 dengue–1 antibody. 0 of 5 patients aged under 10 years developed MVE CF antibody, but 11 of 21 aged 11–20, and 9 of 13 aged 21–30 did. Levels of dengue neutralizing antibody were higher in patients with an MVE CF response. Most patients with CF antibody also developed MVE neutralizing antibody which lasted less than 78 days in 3, but over 4 years in 3 others. CF negative and CF positive patients are considered to have had second and first infections with dengue respectively. The virus which caused the 1954–5 epidemic was closer to dengue–1 than dengue–2 and the most sensitive way of determining this was by neutralizing indices determined in suckling mice.

Paired sera collected from febrile patients at Innisfail 1952–5 and Brisbane 1957–9, were tested. No evidence of dengue or MVE antibody was found in Brisbane children born after the 1942–4 epidemic of dengue, but older age-groups had MVE HI antibody incidences rising from 25 to 66%. About twice as many sera neutralized dengue as MVE and all sera (except 2) with MVE neutralizing antibody also neutralized dengue virus. At Innisfail 12 of 64 sera from children under 11 years of age had MVE HI antibody and the incidence rose to over 80% over 40 years of age. Only 1 of 21 children born after 1945 and bled before the 1954 epidemic had antibody. Sera which neutralized MVE also neutralized dengue virus. Sera collected on the east coast of Cape York Peninsula and on the Atherton Tableland had similar incidences of antibody in relation to all 3 viruses. Sera collected at Coen and near Chillagoe on the other hand, predominantly had MVE rather than dengue antibody. Sera from Townsville where MVE is believed to have caused epidemics gave complex results which were difficult to interpret. MVE antibody was also found in Townsville fowl sera. [For Part I see this *Bulletin,* 1960, v. 35, 381.]

C. E. Gordon Smith

POPE, J. H. & SCOTT, W. **A Survey for Antibodies to Encephalomyocarditis Virus in Man and Animals.** *Australian J. Exper. Biol. & Med. Sci.* 1960, Oct., v. 38, Pt. 5, 447–50.

Sera were tested against 100 LD50 of the Innisfail strain of encephalomyocarditis virus in an intraperitoneal mouse test and later titrated where positive. Sera were collected in Brisbane mainly from patients with aseptic meningitis, from suspected cases of rheumatic fever in the Toowoomba district, and from Innisfail, Cape York, Gulf of Carpentaria and Papua: of 385 human sera only 3 sera had neutralizing antibody (1 German immigrant at Innisfail and 2 Papuans). Of 187 Marsupials of 4 species collected in Queensland only 2 of 50 *Isoodon macrourus* had antibody. 9 of 54 *Rattus rattus* from Queensland and 1 of 6 from Papua had antibody as did 3 of 41 *R. norvegicus* from Queensland. 0 of 24 *R. assimilis,* a rainforest species, had antibody. 2 of 32 *R. sordidus conatus* and 1 of 19 *Melomys lutillus littoralis* had antibody. 7 of 32 *Hydromys chrysogaster* from Queensland but 0 of 11 from Victoria had antibody. 0 of 115 *Mus musculus* had antibody. 1 of 44 horses but none of 30 cats, or of 71 dogs had antibody. *C. E. Gordon Smith*

GIULIANI, G., ANGELA, G. C., BAGLIONE, L. & GALLI DELLA LOGGIA, D. **German Measles: Acute Benign Viral Lymphoreticulosis. The Haemato-Humoral and Histological Aspects of Rubella.** *Panminerva Med.* Turin. 1960, Dec., v. 2, No. 12, 585–602, 51 figs. (38 coloured). [Numerous refs.] [Translation from *Minerva Med.* 1959, v. 50, 4299.]

Epidemics in 1956 and 1959 in Turin provided an opportunity of examining 62 young persons at the height of an attack of rubella.

The main contribution of the present study lies in its analysis of the cytological reaction in the blood-forming organs, particularly as lymph-node biopsy was performed in 3 cases, and aspiration biopsy in another 3. Very good photomicrographs, some in colour, are reproduced.

The enlargement of lymph nodes is the result of hyperplasia of the reticulo-endothelium, so intense as to obliterate the normal pattern of follicles, cords, and sinuses (including even the marginal sinus). Vascular endothelium shares in the process, and swollen endothelial cells are shed into the lumen, and may appear in the peripheral blood. In sections and in aspirated material the proliferating cells are identified as both plasmacytes and lymphocytes, the latter for the most part being atypical, and identical with those to be described in the blood.

The numbers of the various forms of leucocytes in the peripheral blood are not abnormal, except that in some cases (40 out of 62) plasma cells occur and may reach 15% of the total. Atypical lymphocytes always appear, and number from a few dozen to 2,900 per cmm. They possess a hyperbasophilic cytoplasm, and would be described by many pathologists as Türk cells. [An unfortunate mistranslation states that the absence of these cells from the blood should *suggest* a diagnosis of rubella.]

In the marrow the outstanding finding is the presence of up to 50% of mature lymphocytes, only a very small proportion of which are of the atypical form. It is probably this finding that leads the authors to suggest that the hyperbasophilia of cells in the lymph nodes comes about through interference by the virus in their ribonucleoproteins. *Alan B. Raper*

Bacteriology and Immunity

The order in this section is:—**General; Bacteriostatic and Bactericidal Substances; Bacteria; Rickettsiae; Bacteriophages; Viruses; Immunity.**

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-divisions of this section.*

GENERAL

MARSHALL, J. H. & KELSEY, J. C. **A Standard Culture Medium for General Bacteriology.** *J. Hygiene.* 1960, Dec., v. 58, No. 4, 367–72. [10 refs.]

The medium described in this paper is a modification of the CCY medium of GLADSTONE and FILDES [this *Bulletin*, 1940, v. 15, 731]. The basal nutrient medium (casein-yeast-lactate-glucose (CYLG)) has the following composition :—

Casein digest (Oxoid Tryptone)	10 gm.
Yeast autolysate (Marmite)	5 gm.
Sodium glycerophosphate	10 gm.
Potassium lactate (50%, w/w)	10 ml.
Glucose	2 gm.
Inorganic salts solution*	5 ml.
Water to	1000 ml.

Final *p*H 7·0–7·2

* $MgSO_4.7H_2O$, 4·0 gm.; $MnSO_4.4H_2O$, 0·4 gm.; $FeSO_4.7H_2O$, 0.4 gm.; water 100 ml.; acidify with 2 drops of 10 NH_2SO_4.

This medium has good nutrient properties and is suitable for the growth of a wide range of organisms. It can when necessary be readily supplemented. The basic medium is cheap, easy to prepare, reproducible and as fully defined as possible in terms of known nutritional factors. Moreover it can be prepared and stored in concentrated form so that any supplementation required for a special medium, whether in liquid or solid form, can be effected when the concentrate is diluted for use.

The medium described has been routinely used in the Department of Bacteriology in the London School of Hygiene and Tropical Medicine for more than 2 years and has proved to be both reliable and economical.

H. J. Bensted

COLEBROOK, L., LOWBURY, E. J. L. & HURST, L. **The Growth and Death of Wound Bacteria in Serum, Exudate and Slough.** *J. Hygiene.* 1960, Dec., v. 58, No. 4, 357–66, 1 fig. [10 refs.]

The senior author was a colleague of Almroth WRIGHT and Alexander FLEMING. During the First World War these three distinguished workers were continually studying the bacteriology of war wounds, and among a number of interesting obervations they noted that some types of bacteria grew freely from small inocula in fresh serum

but other types grew poorly or not at all (Wright *et al. Lancet,* 1918, i, 831). Certain strains of streptococci and *Staphylococcus aureus* grew readily; these they named "serophytes". Other bacterial types, such as coliform organisms, failed to grow in fresh serum; small inocula appeared to die out. Nevertheless if trypsin were added to the fresh serum, coliform organisms, which they classified as "sero-saprophytes", grew as readily as they did in the exudate of an infected wound. This suggested to Wright and his colleagues that the sero-saprophytic organisms required for their growth some of the breakdown products derived from the proteolytic digestion of serum protein. Alternatively it could be argued that small doses of coliform organisms fail to grow in fresh serum because of certain bactericidal substances; the properdin system is known to be active against many coliform bacilli but inactive against streptococci and staphylococci.

The present authors repeated some of Wright's experiments, using more conventional techniques on selected strains of organisms. They confirmed that both large and small inocula of *Streptococcus pyogenes* and *Staphylococcus aureus* grew well in fresh human serum and that *Escherichia coli* failed to grow from large inocula, and when the inocula were small the organisms were destroyed. If the serum was treated with trypsin or heated at 56°C. for 1 hour the coliform bacilli grew readily; heat plus trypsinization much improved their growth. Heating at 56°C. and treatment with proteolytic enzymes destroys complement and inactivates the bactericidal properties of fresh serum. This was confirmed by using a particular strain of *Shigella sonnei* known to be extremely sensitive to the properdin system. It seems clear therefore that human serum can only become a suitable culture medium for coliform bacilli by the destruction of complement and the inactivation of its bactericidal property, and this change could be brought about by bacterial or leucocytic enzymes. Thus *E.coli* would not be expected to establish itself readily in clean surgical wounds whereas burns or dirty infected war wounds would provide conditions suitable for the multiplication of this organism. In slough material the Gram-negative bacilli actually grew more vigorously than the Gram-positive cocci. *H. J. Bensted*

World Health Organization. Technical Report Ser. No. 200. **Requirements for Biological Substances. 6. General Requirements for the Sterility of Biological Substances. Report of a Study Group. Geneva, 20–25 April 1959.** 31 pp. [Refs. in footnotes.] 1960. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [1s. 9d.; $0·30; Sw.fr.1.-.]

This Study Group examined the sampling methods and the cultural techniques which should be employed before clearing small or large batches of biological material for use. Emphasis was laid on the developing problem of sterility in respect of viruses. The text and an annex set out the conclusions of the Group on such things as temperature and times of incubation, suitable culture media, training of technicians, methods for the detection of bacteria, yeasts and fungi, and viruses. The particular needs of virus vaccines and blood plasma and other substances are dealt with. The text does not lend itself to abstraction and must be examined in the original by all who are concerned with this kind of work. It is a valuable document. *J. W. Howie*

Bate, J. G. **Bacteriological Investigation of Exhaust Air from Hospital Vacuum Cleaners.** *Lancet.* 1961, Jan. 21, 159–61, 2 figs.

A bacteriological study was made of the effluent air from 10 different vacuum cleaners (5 cylinder and 5 tank type) and 3 suction polishers by leading the air stream into a large Polythene bag from which it could subsequently be taken into a slit sampler. The cleaners were examined after they had been in use for some time; their collection bags or chambers therefore contained hospital floor dust. With 9 of the vacuum cleaners the exhaust contained less than 1 bacteria-carrying particle per cu. ft. The less efficient cleaner (a tank type) had only one layer of filtering cloth. The 5 cylinder cleaners all had paper dust-collecting bags. The tank cleaners had various sorts of filter. The air from the the suction polishers yielded 2·8–4·2 colonies per cu. ft. A number of the vacuum cleaners discharged their effluent air in the form of a jet; this was found to raise the bacterial count in the air of an experimental room. Diffusion of the outlet was sufficient to cure this trouble.

In the discussion of these results it is emphasized that the facility with which the cleaner can be emptied without distributing dust is important. A plea is made for the use of piped suction in new hospitals.

R. E. O. Williams

Tartler, G. & Theus, P. M. Experimenteller Beitrag zur Raumluftentkeimung durch Luftfiltration. [**Experimental Contribution to Room Disinfection by Air Filtration**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1960, Nov., v. 6, No. 11, 694–708, 6 figs. [22 refs.]

The air filter tested comprised a layer of glass-wool 30 cm. deep; on the inflow side were dishes containing triethylene glycol, and on the outflow side two ultra-violet lamps. Air was blown through the apparatus at a rate corresponding to about 6 air changes per hour in the test room. Numerous tests were carried out with sprayed suspensions of *Staph. albus, E. coli* and *Bact. subtilis* spores, the air from the two sides of the filter being sampled with slit samplers. The bacterial count was reduced by more than 99% for the first 2 organisms but by only 85–90% for the last. The ultra-violet contributed substantially to the effect. A number of other tests are also reported. *R. E. O. Williams*

Gunsalus, I. C. & Stanier, R. Y. **The Bacteria. A. Treatise on Structure and Function. Vol. I: Structure.**

This book was reviewed on p. 418.

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

The order in this section is:—**General; Antibiotics; colicines; other Therapeutic Substances; Disinfection.**

HERRELL, W. E., BALOWS, A. & BECKER, Jean. **Erythrocillin: A New Approach to the Problem of Antibiotic-Resistant Staphylococci.** *Antibiotic Med.* New York. 1960, Oct., v. 7, No. 10, 637–42.

This paper is from the Lexington Clinic, Lexington, Kentucky. It first reports the sensitivity to 6 antibiotics of 400 recently isolated strains of staphylococci. Those highly resistant to propionyl erythromycin (62 strains were inhibited only by 1000 μgm. per ml. or more) were tested with 2 combinations. Propionyl erythromycin + Oxytetracycline showed some synergy, but propionyl erythromycin + penicillin ("erythrocillin") had a more striking effect. The facts given are that each of 56 strains was resistant to 1000 μgm. per ml. of the former and inhibited only by concentrations varying from 12·5 to >100 units per ml. of penicillin. With both antibiotics present in equal amounts, all but 2 of the strains were inhibited by 3·125 μgm. (or units) per ml. or less. Patients were given these 2 antibiotics separately and together: their serum failed to inhibit the growth of resistant staphylococci after either single antibiotic, but did so after both. Clinical trials of this combination are proceeding. *L. P. Garrod*

HUGO, W. B. & RUSSELL, A. D. **Quantitative Aspects of Penicillin Action on *Escherichia coli* in Hypertonic Medium.** *J. Bacteriology.* 1960, Oct., v. 80, No. 4, 436–40, 1 fig. [17 refs.]

These workers at the Department of Pharmacy, University of Nottingham, cultivated a strain of *Escherichia coli* in a medium containing 0.25% magnesium sulphate, 0.33M sucrose, and 5,000 units/ml. of penicillin (100 and 1,000 units/ml. had similar effects). The course of events in the culture was followed by viable counts, and by total counts (haemocytometer) and diameter measurements of the spheroplasts formed. The main results of these observations was to show that a rapid fall in the viable count preceded spheroplast formation, suggesting that there is a lethal effect independent of interference with cell wall synthesis. *L. P. Garrod*

VARGA, D. T., FOSTER, Frances & WHITE, A. C. **Clinical and Laboratory Studies of Alpha-Phenoxyethyl Penicillin.** *Amer. J. Med. Sci.* 1960, Nov., v. 240, No. 5, 579–86, 5 figs. [11 refs.]

This paper from the University of Louisville School of Medicine, Kentucky, reports the results of tests of the bacteriostatic and bactericidal action of 3 forms of penicillin on 98 recently isolated strains of pathogenic staphylococci. The methods used are not described, the reader being referred for them to another paper [this *Bulletin*, 1960, v. 35, 914]. The results are presented as numbers (in tables) and percentages (in graphs) of strains inhibited or killed by concentrations differing 2-fold from 100 to 0·39 μgm./ml. Larger percentages were susceptible at almost all concentrations to the bacteriostatic action of alpha-phenoxyethyl penicillin (phenethicillin) than to that of penicillins V or G. By analysis of results in accordance with phage types, this difference was shown to be almost entirely due to the greater activity of phenethicillin against type 80/81, to which 45 of the strains belonged: these were highly resistant to other penicillins. There was no corresponding difference in bactericidal action, of which indeed little was seen: only about 10% of type 80/81 and about 40% of the remainder were killed by the highest concentration of each of the 3 penicillins.

The paper also reports a few observations on the concentrations of phenethicillin attained in the blood and other body fluids, and the results of administering it to 20 patients with pneumococcal pneumonia, which were satisfactory except in 2, 1 of whom subsequently responded to tetracycline: the other died and was found to have endocarditis. No ill effects were seen except 2 skin rashes in a total of 40 patients. *L. P. Garrod*

CRIEP, L. H. & FRIEDMAN, H. **Allergy to Phenethicillin.** *New England J. of Med.* 1960, Nov. 3, v. 263, No. 18, 891–3, 2 figs.

This paper confirms by detailed observations made on 2 patients that sensitivity to benzyl penicillin is accompanied by sensitivity to phenethicillin. One was a woman treated for asthma with penicillin in 1953 who reacted violently to the first tablet of phenethicillin prescribed for infectious mononucleosis in 1959. The second was a woman who had had injections of penicillin several years before and reacted to a further injection of "aqueous" penicillin. Both were submitted to scratch tests with solutions of different concentrations of penicillin and phenethicillin and reacted equally to both. The serum of each patient also agglutinated red cells treated with either penicillin or phenethicillin and this agglutination was prevented by the addition of either antibiotic [this *Bulletin*, 1958, v. 33, 1072; 1960, v. 35, 491]. *L. P. Garrod*

HALL, J. W. **Colistin: Analysis of a New Antibiotic in 44 Cases of Systemic Gram-Negative Bacterial Infection.** *Amer. J. Med. Sci.* 1960, Nov., v. 240, No. 5, 561–70. [38 refs.]

Colistin is a polypeptide antibiotic derived from a *Bacillus*, very closely resembling polymyxin B. This paper from the University of Minnesota Medical School, Minneapolis, reviews the literature of this antibiotic, and reports a laboratory and clinical study of it. Tests of the sensitivity to it of 200 strains of bacteria showed *Pseudomonas* and *Escherichia coli* to be almost uniformly sensitive and *Proteus*, staphylococci and streptococci almost invariably resistant: the findings with a few strains of *Klebsiella* and paracolon bacilli were variable. In the form of sodium colistin methanesulphonate, the drug was given to 54 patients intramuscularly 2 or 3

times a day, the total daily dose usually being 75 mgm. (*i.e.*, about 1 mgm. per kgm.). Excluding 10 of these from adjudication for various reasons, the remaining 44, all infected with Gram-negative bacilli of the varieties already named, consisted of 38 infections of the urinary tract, 5 wound infections and 1 pneumonia. The results were good in 29 patients: they are further analysed according to the nature of the infection (it is scarcely surprising that the results were poor in *Proteus* infections) and in accordance with the presence or absence of "major factors adverse to treatment" (*e.g.*, urinary obstruction and severe underlying systemic disease) which had the effect to be expected, particularly in a series whose median age was 60 years. The drug was well tolerated (it is noteworthy that the dosage used was well below the maximum suggested for polymyxin B): only 5 patients showed adverse effects. These were pain on injection in 2, and vertigo, circumoral paraesthesia, and transient azotaemia in 1 each. *L. P. Garrod*

McCabe, W. R., Davis, J. C., Andersen, B. R. & Jackson, G. G. **Furaltadone. A Critical Evaluation of Clinical and Laboratory Studies.** *New England J. of Med.* 1960, Nov. 10, v. 263, No. 19, 927–34, 3 figs. [18 refs.]

Furaltadone (Altafur) is one of several nitrofuran compounds in clinical use as antibacterial agents: it differs from the others in that a systemic effect is claimed for it. These authors from Chicago have made both a laboratory and clinical study of its action. Of 64 strains of staphylococci, 32 (50%) required a concentration of 7·8 μgm./ml. of furaltadone to inhibit their growth, the remainder, concentrations of from 1 to 15·6 μgm./ml. The drug is slowly bactericidal, but 10-fold dilution with normal medium of a culture in which bactericidal action is occurring results in immediate re-growth. The drug was estimated in the blood of patients 2, 4 and 6 hours after a dose. When 200 mgm. was given orally the amounts found were very variable: the mean concentrations at the intervals named were 2·1, 1·4 and 0·2 μgm./ml., but in 60, 78 and 88% of specimens respectively, none could be detected. Higher and steadier levels were attained after intravenous infusion of 1 or 1·5 gm., but even after this some specimens contained none at 6 hours.

Oral treatment was given to 20 patients and intravenous to 8: all had staphylococcal infections, in the form of septicaemia or endocarditis in 11, wound infection in 8, pneumonia or empyema in 6, osteomyelitis or pyarthrosis in 2 and meningitis in 1. The results were generally unsatisfactory, only 8 patients (29%) apparently responding to treatment. In 2 a serious extension of the infection, to a joint and the blood stream, actually occurred during treatment. Comparison of the serum concentrations attained, the concentration required to inhibit the infecting staphylococcus, and the results of treatment, suggest that simple failure to produce an adequate drug level in the blood to act on the infecting organism was a probable cause of failure.

Toxic effects included nausea and vomiting (fairly common), eosinophilia, and single examples of skin rash, leucopenia, fever and temporary renal impairment (some of these possibly due to other medication). "The results permit no confidence in furaltadone as treatment for serious staphylococcal infections in the majority of patients." *L. P. Garrod*

Mast, W. H. **Neuropathy due to Furaltadone.** *New England J. of Med.* 1960, Nov. 10, v. 263, No. 19, 963.

A woman aged 40 was treated with furaltadone for staphylococcal sepsis of traumatic wounds: the dose was 1 gm. daily to a total of 21 gm. in 3 short courses. During the third of these she had diarrhoea and a burning sensation in the skin of the hands and feet, followed by dysphagia, aphonia, diplopia, facial paralysis and paralysis of the tongue on the right side, and left foot drop. These effects were regarded as due to peripheral neuritis. Slow recovery followed the withdrawal of the drug, but was not complete 6 weeks later (apparently the time of writing). *L. P. Garrod*

Malizia, W. F., Gangarosa, E. J. & Goley, A. F. **Benzalkonium Chloride as a Source of Infection.** *New England J. of Med.* 1960, Oct. 20, v. 263, No. 16, 800–802.

This report from the Walter Reed Army Hospital, Washington, records very similar findings to those of Plotkin and Austrian [this *Bulletin*, 1958, v. 33, 1076], whose warning seems therefore not to have been heeded universally. A series of apparent blood stream infections was traced to the antiseptic used for disinfecting the skin before venepuncture etc.: this was benzalkonium chloride (Zephiran) in a concentration of only 1 in 750, and the pieces of gauze used for its application were kept soaking in it. Fabrics adsorb disinfectants of this class and thus inactivate the solution. The 11 patients involved, from 10 of whom blood cultures were positive, were all seriously ill from other diseases. As in the previous report, the fact that the incriminated method of disinfecting the skin was used before blood culture casts some doubts on the results of this, but the authors regard the evidence of true infection as "definite" in 4 cases, although only "probable" in 4 and doubtful in 3. Large abscesses developed in 2 patients, whose histories are given. The organism in these, in all the blood cultures and in the incriminated solution was identified as *Aerobacter cloacae* [*Cloaca cloacae*]. It was also found in a bottle of the same solution from the hospital pharmacy. When culture of it was added to the solution the organism was irrecoverable after 15 minutes, but when gauze was present it survived up to 4 weeks.

[The authors explain the discrepancy between survival in a stock bottle and its bactericidal action on added organisms by suggesting that these organisms "are capable of adapting to this particular germicidal environment", but they offer no evidence of this. They do not say what closure was used for the bottles: it has been shown that re-contamination can occur from bark corks whenever these are removed (Anderson and Keynes, *ibid.*, 1162).] *L. P. Garrod*

HORN, Ilse M. Die chemische Desinfektion des Influenzavirus unter besonderer Berücksichtigung der in der DDR gebräuchlichen Desinfektionsmittel. **[Chemical Disinfection of Influenza Virus with particular Reference to Disinfectants available in Western Germany]** *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1960, Oct., v. 6, No. 10, 643–59. [20 refs.]

These experiments were done with 4 strains of influenza virus (not distinguished in tables of results) and by 3 methods. In one, infected allantoic fluid was simply mixed with dilutions of disinfectant: a second was similar except for the addition to the mixture of egg albumen: the third was a "carrier method", small squares of fabric being soaked in virus suspension and used for the test, apparently without being dried. After 5, 10 or 20 minutes, the mixtures were suitably diluted and eggs inoculated, survival of the virus being indicated by the development of haemagglutinin.

The disinfectants tested were 6 pure substances and 17 proprietary compounds, the composition of which is described only in general and often rather vague terms. The detailed results occupy pages of tables, and can only be outlined. Formalin and 2 products containing it were effective in all 3 tests, as was ethanol and (more rapidly) Optal, which is *n*-propylalcohol. Phenol was effective at 2% except in the carrier test: 12 proprietary phenolic disinfectants performed in general fairly well, but with some failures in 1 of the tests, such as Septygeen (described only as a "solution of different oxybenzol derivatives"), which failed in the presence of egg albumen. 2 quaternaries also performed better in the simplest form of test than in the others: no attempts seem to have been made to neutralize either these or mercury perchloride, a 0·1% solution of which is shown as killing the virus in 2 minutes under all conditions. 0·25% chloramine was consistently effective, as was 0·5% potassium permanganate except in the presence of egg albumen. The author concludes that formalin, certain phenolics, chloramine and Optal are suitable for purposes involving destruction of influenza virus. *L. P. Garrod*

BACTERIA

The order in this section is:—Cocci; Donovania; Mycobacterium; Corynebacterium; Haemophilus; Pseudomonas; Pfeifferella; Enteric Organisms; Brucella; Pasteurella; Bacillus; Anaerobes; Spirochaetes; Erysipelothrix; Listeria; Others.

EKSTEDT, R. D. & YOTIS, W. W. **Studies on Staphylococci. II. Effect of Coagulase on the Virulence of Coagulase Negative Strains.** *J. Bacteriology.* 1960, Oct., v. 80, No. 4, 496–500. [11 refs.]

The authors continue their work on the effect of coagulase on coagulase-negative staphylococci *in vitro* [this *Bulletin*, 1960, v. 35, 387] by studying its effect *in vivo*.

Washed suspensions of organisms were prepared containing $5{\cdot}3 \times 10^8$ viable cells and 0·03 ml. of such suspensions were injected intracerebrally into batches of mice. There was a 50% mortality or more after 3 days in mice injected with one of 15 out of 16 coagulase-positive strains. Death was due to extensive brain abscesses. There were no deaths after 14 days in mice injected with one of 6 out of 9 haemolytic coagulase-negative strains.

Partially purified coagulase prepared by the method of TAGER [*ibid.*, 1949, v. 24, 906] contained 0·005 mgm/ml. coagulase. This was heated at 60°C. for 30 minutes to destroy the alpha toxin and mixed in 0·2 ml. amounts with 5·0 ml. of standard suspensions of 3 coagulase-negative strains. 0·03 ml. was injected intracerebrally into mice. In 5 experiments cells or coagulase produced no deaths after 14 days while cells with added coagulase produced between 37·3% and 55·5% mortality.

Cells centrifuged after exposure to coagulase and resuspended in distilled water before inoculation also showed enhanced virulence but cells suspended in human serum, egg albumen or dextran were avirulent. Coagulase did not enhance the virulence of Group A streptococci nor did it enhance the virulence of coagulase-negative staphylococci if it was injected intravenously immediately before intracerebral challenge. The coagulase was titrated in terms of virulence enhancement but with the 2 strains used this was not such a sensitive test as the ability to clot plasma.

The authors suggest that coagulase acts as a surface antigen inhibiting phagocytosis and that its adsorption to coagulase-negative staphylococci may confer some form of protection in the early stages of the establishment of infection. *M. Patricia Jevons*

WOODIN, A. M. **Assay of the Two Components of Staphylococcal Leucocidin and their Antibodies.** *J. Path. & Bact.* 1961, Jan., v. 81, No. 1, 63–8.

RICHOU, R. Les enzymes des filtrats de culture du staphylocoque. **[Enzymes of Culture Filtrates of Staphylococci]** *Bull. Acad. Nat. Méd.* 1960, v. 144, No. 35, 842–6.

FOSTER, W. D. & HUTT, M. S. R. **Experimental Staphylococcal Infections in Man.** *Lancet.* 1960, Dec. 24, 1373–6, 1 fig.

The epithelium was removed from a small area on the skin of the forearm by scraping with a scalpel and the

area, in which capillary loops were visible but which did not bleed, was inoculated with about 10^6 staphylococci. The lesion was covered with a coverslip sealed on to the skin with Sellotape. Subsequently the lesions were moistened and sampled with alginate-wool swabs.

After 27 hours, a lesion under a coverslip yielded 55×10^6 staphylococci compared with $0{\cdot}7 \times 10^6$ in a comparable lesion swabbed at 0 hours. An uncovered lesion showed practically no increase in count. The addition of french chalk or starch as a foreign body had no effect. Cytologically the lesions showed a predominance of polymorph leucocytes. There was no noteworthy difference between the lesions produced by five different phage types of *Staph. aureus*. The smallest dose found to produce a lesion was about 15 viable units of staphylococci; 6×10^6 cocci were recovered from this lesion 24 hours after the start of the experiment.

During the course of these experiments 2 of the 3 volunteers developed boils on different parts of the body which yielded staphylococci of the same type as the strain used in most of the experiments; 1 also became a nasal carrier of the strain. *R. E. O. Williams*

McCune, R., Dineen, P. & Batten, J. C. **The Influence of Antimicrobial Agents on Total Populations of Staphylococci in Animal Tissues.** *J. Immunology*. 1960, Nov., v. 85, No. 5, 447–64, 22 figs.

Batches of mice were infected intravenously with one of 2 strains of *Staphylococcus aureus*—Giorgio, a penicillin-resistant strain, and Wolbeck, a penicillin-sensitive strain. At appropriate intervals mice were killed and lungs, spleen and kidneys were homogenized. Numbers of staphylococci in an organ were assessed as the number of culturable units per ml. of homogenate [see McCune and Tompsett, this *Bulletin*, 1957, v. 32, 699].

The Giorgio strain was the more virulent. Maximum population increase occurred with both strains in the kidneys during the first week and macroscopic lesions were present after 2 days. There was a rapid reduction of organisms in the spleen and in the lungs of Wolbeck animals. The lungs of the Giorgio animals occupied an intermediate position.

The influence of immediate and delayed (54 hours) therapy with penicillin, streptomycin, tetracyclines, novobiocin and erythromycin on infected animals was then studied and figures are given showing counts in the 3 organs over a 30-day period, for all treatments.

Penicillin treatment of animals infected with the Giorgio strain prolonged survival and slightly reduced staphylococcal counts in spite of the *in vitro* resistance of this strain. In general, delay in starting therapy had no effect on the influence of penicillin, tetracycline or erythromycin but it did in the case of streptomycin and novobiocin in the kidneys.

Penicillin in combination with the other antibiotics was next studied and results suggested an antagonism between penicillin and other drugs in the treatment of Giorgio animals. This was usually most apparent after the first 2 weeks of therapy.

Results show that the course of infection in mice by these 2 strains in the 3 organs is predictable with and without treatment and the authors discusss them and compare them with results they obtained with *Mycobacterium tuberculosis* [*loc. cit.*]. *M. Patricia Jevons*

Lancaster, L. J. & Sherris, J. C. **An Agar-Diffusion Grouping Technic for Beta Hemolytic Streptococci.** *Amer. J. Clin. Path.* 1960, Aug., v. 34, No. 2, 131–2.

A micro agar diffusion method for grouping β-haemolytic streptococci is described. 3% agar in normal saline is pipetted onto a slide to a depth of 2–3 mm. 5 holes 2 mm. in diameter into which grouping sera are placed, surround a central antigen hole containing a Lancefield extract of the strain under test. Tests were read after 1, 4, 24 and 48 hours' incubation at 37°C. in a wet chamber. A positive test consisted of a precipitation line with the appropriate antiserum.

Lancefield extracts of 79 strains of various groups were grouped by this method and the capillary tube test [Swift, *et al.*, this *Bulletin*, 1944, v. 19. 67]. 75 were groupable by the diffusion method, 22 of them in the 1st hour and 49 by the 4th hour compared with only 68 by the capillary method, 6 of which results were interpreted differently by 3 observers. The authors conclude that the diffusion method is more economical, more sensitive and easier to read than the capillary method.

[In Britain the ring precipitin test for grouping is used in preference to the capillary test in the majority of laboratories. In this simple test the result is read in 5 minutes. The authors do not report any false positive results in their work. One might expect to find additional lines of precipitation due to protein antigens after 48 hours' incubation. Grouping serum of high titre would seem to be necessary if these are to be avoided.]

M. Patricia Jevons

Cremer, Natalie & Watson, D. W. **Host-Parasite Factors in Group A Streptococcal Infections. A Comparative Study of Streptococcal Pyrogenic Toxins and Gram-Negative Bacterial Endotoxin.** *J. Exper. Med.* 1960, Dec. 1, v. 112, No. 6, 1037–53, 6 figs. [22 refs.]

Sonic extracts of *Streptococcus pyogenes* are pyrogenic in rabbits and induce tolerance to repeated injection, especially in respect of the second part of the biphasic temperature peak. A pyrogenic response was also induced by extracellular material from a type 18 strain, and there was only partial reciprocal tolerance between this and the intracellular pyrogen. There was no reciprocal tolerance between the extracellular pyrogen of the streptococcus and a *Salmonella typhi* pyrogen; there was however some, irregularly reciprocal tolerance with the intracellular material and *Salm. typhi*. It is suggested that the streptococci produce 2 pyrogenic toxins: one a non-type-specific intracellular material and the other an extracellular material, showing some type-specificity [see Watson, this *Bulletin*, 1960, v. 35, 694], which is neutralized by antiserum. Neither is identical with the pyrogenic endotoxin of Gram-negative bacteria.

R. E. O. Williams

KUHARIC, H. A., ROBERTS, C. E., Jr. & KIRBY, W. M. M. **Tetracycline Resistance of Group A Beta Hemolytic Streptococci.** *J. Amer. Med. Ass.* 1960, Dec. 3, v. 174, No. 14, 1779–82. [18 refs.]

Of 218 strains of Group A haemolytic streptococci recently isolated in Seattle, Washington, 42 (20%) were resistant to tetracyclines: none was resistant to penicillin, erythromycin, chloramphenicol or bacitracin. Strains were regarded as tetracycline-resistant when the minimum inhibitory concentrations of tetracycline and demethylchlortetracycline were 4 and 2 μgm/ml. respectively or more, the normal findings being 0·1 and 0·05 μgm./ml. Resistance persisted after 10 transfers in normal medium. All the strains were also typed: of the 42 resistant strains 11 were of type 12, 3 of type 4 and the rest untypable. (Typing results for the sensitive strains are not given: in the absence of this information it remains conjectural whether tetracycline resistance is characteristic of particular types.)

Some of these strains came from cases of throat infection which had failed to respond to tetracycline treatment; brief particulars of 4 are given. 2 patients are mentioned whose fathers were found to have a similar organism in their throat; one of these fathers was a physician and a symptomless carrier, the other a man "on intermittent long-term prophylactic tetracycline therapy for chronic lung disease". It is concluded that tetracycline should not be used for prophylaxis of rheumatic fever, or for the treatment of streptococcal sore throats unless the sensitivity of the strain has been verified. *L. P. Garrod*

BARKER, S. A., BRIMACOMBE, J. S., HOW, M. J., STACY, M. & WILLIAMS, J. M. **Two New Amino-Sugars from an Antigenic Polysaccharide of *Pneumococcus*.** [Correspondence.] *Nature.* 1961, Jan. 28, v. 189, 303–4. [12 refs.]

BERGER, U. & WULF, B. Untersuchungen an saprophytischen Neisserien. [**Studies on Saprophytic Neisseriae**] *Ztschr. f. Hyg. u. Infektionskr.* 1961, v. 147, No. 3, 257–68. [24 refs.]

INST. MÉD. TROP. PRINCE LÉOPOLD. Premier colloque international sur les mycobactéries, 4, 5 et 6 Decembre 1959 (organisé avec l'aide du Ministère de l'Instruction Publique) [JANSSENS, P. G., Editor]. [**First International Conference on Mycobacteria**] 198 pp., illustrated. [Numerous refs.] 1960. Antwerp, 155 Rue Nationale.

This colloquium was held in Antwerp on 3 days. The papers were read in groups and at the end of each there was a discussion which is reported verbatim.

L. M. G. GEURDEN, *Introduction to the study of mycobacteria and mycobacteriosis* (pp. 2–7). In this introduction the mycobacteria were classified and a brief summary was given of the methods used in studying them and the diseases they produce; special attention was given to the "anonymous bacilli".

A. DEVOS, *The techniques for isolating mycobacteria* (pp. 8–15). The media used since Koch first grew the tubercle bacillus on coagulated bovine serum in 1884 were recounted, and the roles of some of the ingredients were mentioned, *e.g.*, the necessity for growth of manganese and iron, the buffering action of phosphates, the solubilizing effect of citrates on certain organic salts, the accelerating action of asparagine and cholesterol, and the detoxicating action of albumin. The methods of destroying contaminating non-acid fast bacilli were summarized, and the impossibility of choosing an ideal general method is emphasized, the choice depending on the mycobacterium, the pathological specimen source and on the number and type of contaminating organisms.

I. W. LESSLIE, *Purified protein derivatives prepared from non-tuberculous mycobacteria including Mycobacterium johnei* (pp. 16–25). This paper was concerned with non-specific tuberculin reactions in cattle. 2·5% of cultures of 5,000 specimens, mainly from the udder, yielded rapidly growing acid-fast bacilli, the commonest being *Myco. smegmatis,* and tuberculins from these organisms were tested in guineapigs and cattle sensitized with the various bacilli. Except for *Myco. smegmatis,* the reactions in the guineapigs were stronger with homologous than with heterologous sensitization; PPD from *Myco. smegmatis* was found to react as strongly in animals sensitized with human and bovine tubercle bacilli as in those sensitized with *Myco. smegmatis.* Cows infected intramammarily with the various mycobacteria developed homologous allergy only. In guineapigs sensitized with *Myco. balnei,* the homologous PPD was some 20 times at potent as human PPD. Tests with avian and *Myco. johnei* PPD in guineapigs showed that in homologous sensitization, homologous avian PPD is 6 times as potent as *Myco. johnei* PPD, and homologous *Myco. johnei* PPD is 2·9 times as potent as avian PPD, but in sensitized calves these differences were less marked. The author concluded that the existing evidence does not suggest that the saprophytic mycobacteria are a common cause of non-specific reactions to mammalian tuberculin, but sensitization may be caused by the intermediate types such as *Myco. balnei.*

P. HAUDUROY, *Attempt to classify the mycobacteria* (pp. 36–51). The author discussed the unsatisfactory state of the classification of mycobacteria, a state which has partly arisen from the duplicating of the names and the fact that cultures were often impure. The "anonymous" mycobacteria were discussed, and the unsatisfactory state of using pigmentation as the basis for their classification was emphasized.

The author concluded by recommending that a group of experts make a complete study of these strains and establish an acceptable classification.

G. PENSO, *The identification of the mycobacteria in the light of their antigenic constitution* (pp. 52–70). The antigenic structure of mycobacteria as revealed by phage sensitivity tests was mentioned, followed by a detailed description of the antigens. The bacilli were disintegrated mechanically at −60°C., and antisera to them were prepared in rabbits. 11 species were examined and a common antigen was detected in each; the bovine tubercle bacillus proved the most complex for it contained 10 different antigens; the human bacillus contained 9 antigens all of which were present in the bovine type, and the avian tubercle bacillus had 5 antigens, 4 of which were present

in the mammalian types. Each of the other species had a specific pattern of antigens, but they all contained 2 or more antigens of the tubercle bacilli. The least complex species was *Myco. phlei*, which had 5 antigens. Sensitivity to a particular phage was found to be related to the presence of a common antigen.

J. Asselineau, *Composition of the peripheral part of the tubercle bacillus* (pp. 71–84). The author discusses the cord factor, the cell wall and the D waxes. Although the cord factor plays no special role in cord formation it is the only toxic factor isolated from the tubercle bacillus, and degradation and synthesis studies show it to be a dimycolate of trehalose. The cell wall consists essentially of a glyco-peptide containing arabinose, galactose and a small proportion of mannose as well as glucosamine, muramic acid, alanine, glutamic acid and α,ϵ-diamino-pimelic acid. Comparison of the constituents of the D waxes and the cell walls, including those of *Nocardia* and of other mycobacteria, show that they are very similar; the D waxes are thus probably a constituent of the wall, this would account for some of the properties of the tubercle bacilli, *e.g.*, their hydrophobic nature and their fixation of neutral red.

G. Pallaske, *On the question of tissue reaction in animals infected with mycobacteria and the determining factors* (pp. 93–108). The reactions to the tubercle bacillus are essentially proliferative or exudative. In the horse, swine, monkey, giraffe, mouse, rat, hedgehog, hamster and sometimes in the guineapig, the response is mainly proliferative but the exudative form is typical for the bovine and caprine. The multifarious pathological aspects depend on variations in the bacillus and the host, immunobiological and allergic conditions being important variations in the latter.

Of the other mycobacterial infections, Johne's disease is remarkable for its specificity, for the intestine and mesenteric glands, its chronicity and invariable fatal outcome, and the cutaneous nodules of the bovine which have been studied in the U.S.A., and bear some resemblance to nodular leprosy, always contain acid-fast bacilli, but they never prove to be tubercle bacilli. Although cervical adenitis of swine resemble tuberculosis, tubercle bacilli have never been found in the lesions, and Roeckl's granuloma is also not tuberculous.

Ch. Gernez-Rieux, *The serological diagnosis of mycobacterial infections* (pp. 111–126). The various serological methods are reviewed and the haemagglutination and haemolytic method are considered to be the most sensitive although the titres vary with the species of red cells used; the haemolytic method is the more sensitive and although positive results to titres of 1:8 in infants and 1:16 in adults occur in non-tuberculous subjects and there are cross-reactions with other mycobacterial infections, the method is valuable. Precipitation reactions have not as yet been used for diagnosis.

J. Mortelmans, *Mycobacterial infections of animals in the Congo and Ruanda-Urundi* (pp. 130–140). Human tuberculosis has been present for a long time in the Congo, but animal tuberculosis and Johne's disease is very sporadic and controlled by the Veterinary Service; in Ruanda-Urundi human and bovine tuberculosis are widespread. Tuberculin testing of indigenous cattle is complicated by false-reactions and only the intradermal test is of value.

H. Huitema, *PPD tuberculin and tuberculin tests in cattle* (pp. 148–163). Tuberculin testing is the only available procedure that can lead to the eradication of tuberculosis. The author used PPD supplied as a liquid concentrate and he discusses the methods of standardization in guineapigs and cattle. Specificity is checked in cattle sensitized with avian tubercle bacilli and *Myco. johnei*, and an adequate proportion of A and B tuberculins to C tuberculin is ensured by adding Zn, Co and Mn to the culture media. Tween 80 in the ampoule minimizes adsorption on to the glass. Avian tuberculin is used only when there is doubt about the reaction.

Human tubercle bacilli do not produce macroscopic lesions in cattle, but the avian tubercle bacilli which usually cause none or only slight disease may occasionally produce serious disease. The author discussed the possible causes of non-specific reactions, some of which appear to be due to non-mycobacterial infections, *e.g.*, actinomycosis, actinobacillosis and echinococcosis.

M. J. Quertinmont, *Wounds with acid-fast bacilli* (pp. 168–178). A necrotic ulcer, caused by an acid-fast bacilli and occurring most frequently in children of Maniema, Congo, was described. The disease occurs in 2 forms; in one the lesions are limited to the ulcer which is really secondary to an acute necrotizing dermatitis, and in the other there is also osteitis and arthritis.

Growth of the organisms in primary culture takes 6–10 weeks on Löwenstein medium at 32°C.; no growth occurs at 37°C. or on ordinary media. Growth in secondary culture takes 8 days and its colour is white or cream-yellow. No lesions are produced in guineapigs, but in the rat the bacilli produce lesions in the scrotum and death in $2\frac{1}{2}$–5 months. The organisms are resistant to all drugs and excision of the lesions is the only effective treatment.

S. R. Pattyn and J. P. Delville, *Histological aspect of the ulcers of BAR* (pp. 178–180). The histological examination of 15 biopsies of the ulcers are described, and tuberculosis and leprosy are considered to be excluded.

F. Scatozza and G. Mondino, *Attempt to grow tubercle bacillus on HeLa cells* (pp. 182–188). This paper is a short account of the authors' successful attempt to grow tubercle bacilli in HeLa cells. Human, bovine and avian grow intracellularly for 4 days. The mammalian strains grew in cords and although the avian strain also have a parallel arrangement, it is much looser.

S. R. M. Bushby

Chodosh, S. & Gray, J. B. **A Cultural Study of Acid-Fast Microorganisms concentrated by Hydrocarbon-Adsorption and Sedimentation Methods.** *Amer. Rev. Respiratory Dis.* 1960, Nov., v. 82, No. 5, 695–703. [52 refs.]

The authors had previously described a method (*Amer. Rev. Tuberculosis*, 1959, v. 79, 830) in which tubercle bacilli were collected from homogenized sputum onto a coverslip with a siliconized layer by merely dipping the coverslips into the homogenate, advantage having been taken of hydrophobic and lipophilic nature of the bacilli. They now report on a method in which a sphere of solid paraffin, 2 mm. in diameter, was added to specimens of sputum treated with trisodium phosphate. After centrifuging, the wax ball was rolled over the surface of Peizer medium and the growth and its degree of cording obtained

were compared quantitatively with that of a similar tube of the medium inoculated from the deposit of the specimens.

Of the 240 specimens examined, 95 were positive for mycobacteria and 5 for *Nocardia*. Of the specimens positive for mycobacteria, 73·7% were positive by both methods, 92·6% being positive from the deposits and 81·0% by the paraffin method. 10·8% of the cultures from the deposits were contaminated as compared with 1·25% from the paraffin. 73% of the paraffin method cultures showed significantly more cording than did the corresponding culture from the deposit, and in 35% of these paired cultures the culture from the deposit grew bacilli that were either poorly corded or completely disorientated.

Although the cultures from the deposit yielded the greater number of positive results, the higher yield of strongly corded bacilli from the paraffin method suggests that this method selects the more virulent bacilli, presumably owing to the bacilli having a lower specific gravity and a higher affinity for the hydrocarbon.

S. R. M. Bushby

TARSHIS, M. S. **A Comparative Study of the Aniline-Cyanogen Bromide and O-Tolidine-Cyanogen Bromide Direct Qualitative Microniacin Tests for Differentiating Human Tubercle Bacilli from other Mycobacteria. Results obtained using Fresh Cultures.** *Amer. Rev. Respiratory Dis.* 1960, Nov., v. 82, No. 5, 733–5.

In both of these methods the niacin was extracted by flooding the growth on Tween-albumin niacin test medium with 2–10 drops of distilled water, the quantity depending on the amount of fluid already present, and then after 5 minutes the water was removed. After sterilizing by autoclaving at 15 lb. per sq. inch for 15 minutes, 2 drops of the extract were placed into 2 depressions in a white glazed porcelain spot plate and 1 drop of 4% aniline in 95% ethanol was added to one, and 1 drop of 1·5% *o*-tolidine in 95% ethanol, to the other; to both mixtures 1 drop of 10% aqueous cyanogen bromide was then added. The plate was rocked to mix the ingredients and the results were read 5 minutes later, with a reflected fluorescent light. The colour of a positive result with the tolidine mixture was coral red and was yellow with the aniline mixture, the intensities of the colour depending on the concentration of niacin.

9 strains of human tubercle bacilli were positive by both methods, whereas 1 of 2 bovine strains, 2 avian, 6 unclassified mycobacteria and 2 saprophytes gave negative reactions. The bovine strain that gave a positive result was the Ravenel strain and this reaction was weak and became positive only after 14 days' incubation. With cultures that were 7–10 days old the aniline method was slightly more sensitive than the tolidine method, but with older cultures there was no difference between the methods.

[See also GUTIÉRREZ-VÁZQUEZ, this *Bulletin*, 1960, v. 35, 808.] *S. R. M. Bushby*

MATKOVICS, B., KOVÁCS, E. & FÖLDES, J. **Investigation of the Oxidation-Reduction Potential in *Mycobacteria*.** *Enzymologia.* The Hague. 1960, Dec. 31, v. 22, No. 5, 273–6, 1 fig.

(L.268)

VILKAS, Erna & LEDERER, E. Sur la structure du phosphatidyl-inosito-dimannoside de *Mycobacterium tuberculosis*. [**Structure of the Phosphatidyl-Inosito-Dimannoside of *Mycobacterium tuberculosis***] *Bull. Soc. Chimie Biol.* 1960, v. 62, Nos. 9/10, 1013–22. [20 refs.]

MUKHERJEE, S. L., NAHA, J. & CHATTERJI, R. C. **Studies in Sulfur Metabolism of *Mycobacterium tuberculosis*, H37Rv Strain, and Development of a Synthetic Medium designated as " M-Medium ".** *Amer. Rev. Respiratory Dis.* 1961, Jan., v. 83, No. 1, 117–20. [19 refs.]

BEKIERKUNST, A. & ARTMAN, M. **Studies of *Mycobacterium tuberculosis* H37Rv grown *in vivo*: Inhibitor of Lactic Acid Dehydrogenase in Normal and Infected Mice.** *Proc. Soc. Exper. Biol. & Med.* 1960, Dec., v. 105, No. 3, 605–9, 1 fig.

ARTMAN, M. & BEKIERKUNST, A. **Studies of *Mycobacterium tuberculosis* H37Rv grown *in vivo*: Utilization of Glucose.** *Proc. Soc. Exper. Biol. & Med.* 1960, Dec., v. 105, No. 3, 609–12.

NISSEN-MEYER, S. **Epidemiologic Studies of Tuberculin Sensitivity. III. Estimation of Prevalence of Mycobacterial Infection from Results of Skin Tests with Mycobacterial Antigens.** *Amer. J. Hyg.* 1960, Sept., v. 72, No. 2, 169–94, 3 figs. [16 refs.]

The U.S. Public Health Service have been carrying out programmes of skin testing for sensitivity to various types of tuberculin. A relatively strong sensitivity to tuberculin prepared from the human type of tubercle bacillus can be acquired from infection with the disease-producing type of tubercle bacillus. A lower sensitivity may be caused by other types of mycobacterium, differing from the human type by a low disease-producing capacity. This latter type of sensitivity has a higher prevalence in the south-eastern than in the north-western areas of the United States. The analysis of the material produced by such programmes involves a number of problems, the theoretical basis of which is discussed in great detail. The method adopted rests on two main assumptions. First that the observed test results originate from the same infecting agent in all populations and that the number of different types of infection is known. Second, the hypothetical distribution of test results given by any agent or combination of agents must be at least approximately the same in all populations regardless of the prevalence of the particular type of infection in the population.

The present material for analysis was obtained from 57,923 white recruits coming to the Great Lakes Training Centre. The recruits were from 17 to 21 years of age and had lived all their lives in the U.S.A. Each recruit was given 4 skin tests, the testing material being (1) PPD-S (human tubercle) in 5 tuberculin unit doses and (2) PPD-B obtained from an atypical strain of mycobacterium—

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Battey's bacillus [this *Bulletin*, 1957, v. 52, 659], which is non-pathogenic for the guineapig, and is closely related to the agent responsible for most of the cross-reactions in PPD-S in the southern regions of the U.S.A.

These two infecting agents will give 4 mutually exclusive infection groups, *i.e.*, 2 groups infected by only one agent (Group S and Group B), a non-infected group and a group infected by both agents. These reactions were classified into 3 categories of reaction to each antigen, corresponding to definitely negative reaction, small, intermediate and large reactions.

It was found that PPD-B gives larger reactions in S-infected cases than PPD-S does in B-infected cases. In other words PPD-B is a less specific antigen or it has a wider antigenic spectrum than PPD-S.

The recruits were allocated to the State given as their home address. The prevalence of S infections was the highest in those States which have the highest death rate from tuberculosis in recent years. It did not have the marked geographical variation that B infection had, *i.e.*, increasing from north-west to south-east.

The assumptions underlying the analysis may not be completely fulfilled. The group B apparently comprises subjects infected by different agents, more closely related to each other and to the Battey organism, than to agent S but differing in their capacity to produce reactions to PPD-B.

[For earlier parts, see this *Bulletin*, 1960, v. 35, 916.]

Charles L. Sutherland

FARR, R. S. & BLOCH, H. **The Binding Capacity of Tuberculous and Nontuberculous Human Serum for ^{131}I-Labelled Extracts from Tubercle Bacilli.** *Amer. Rev. Respiratory Dis.* 1960, Nov., v. 82, No. 5, 687–94, 1 fig.

The antigens used in this study were derived from H37Rv by disintegrating the bacilli by grinding with glass powder and sonic oscillation, and then freeze-drying after millipore filtration. The antigens were labelled with ^{131}I by the method of TALMAGE *et al.* [this *Bulletin*, 1952, v. 27, 616].

The binding capacity of serum was measured by adding an excess of unlabelled antigen to 0·5 ml. 1:40 diluted serum and adding 0·5 ml. of borate buffer to a similar volume of the serum; to both tubes an excess of labelled antigen was then added. After incubating overnight at 4°C. the globulins were collected by precipitation with anti-globulin serum. The percentage of ^{131}I precipitated from the tube containing the borate buffer less that in the tubes containing the unlabelled antigen, was taken as percentage of ^{131}I activity specifically bound by antibodies; the activity in the tube to which had been added antigen was regarded as non-specific binding of labelled antigen because the antibodies were presumably blocked with the unlabelled antigen.

Early results showed that although different batches of labelled antigen varied in their binding characteristics for tuberculous and non-tuberculous sera, their relative differences were constant. The results obtained with the sera were therefore expressed as the ratio between the percentage activity absorbed by the test sera and that absorbed by a negative serum with high binding capacity. 151 sera were examined and the results showed: (1) that a ratio above 1·2 was indicative of active tuberculosis and was observed in 40% of the serum from cases of active tuberculosis; (2) a ratio between 0.9 and 1.2 was indicative of at least a 50% chance that the serum came from a case of active tuberculosis; and (3) that a ratio of less than 0·9 was non-informative.

As only crude bacterial extracts were used and as some of the antigens may have been labelled preferentially, the authors emphasize the need for further work with purified antigens. *S. R. M. Bushby*

LAMBERT, H. P. **The Influence of Chemoprophylaxis on Immunity in Experimental Tuberculosis.** *Amer. Rev. Respiratory Dis.* 1960, Nov., v. 82, No. 5, 619–26, 1 fig.

The experiments described in this paper were designed to show whether an animal's immunity continues to increase for a number of weeks after it has been infected with tuberculosis or whether the maximum protection is reached soon after infection, and whether isoniazid administered after immunity has developed, interferes with the immunity.

In the 3 experiments, mice were infected intravenously with a small dose of living tubercle bacilli (13–130 viable units) and 8, 16, 24 and 28 weeks later they were challenged with a larger inoculum (5×10^3–$7{\cdot}4 \times 10^4$ viable units). Immunity was assessed by the number of bacilli grown from the spleen and lungs 3–6 weeks after challenge as compared with the number present in these organs of mice not given the primary infection. Some of the mice were treated daily with 4–5 mgm. isoniazid per kgm. from the 8th week to the day of challenge or to 2 weeks before that day; this dose of drug was sufficient to suppress the primary infection almost completely.

The results showed that immunity was well established by the 8th week and that it neither increased after that time nor was it affected by the treatment with isoniazid, starting from the 8th week. None of the tubercle bacilli recovered from the spleen was resistant to isoniazid, a finding which the author interprets as evidence that the bacilli of the primary inoculum were already in a quiescent phase by the time the treatment was started. These results are discussed in relation to the possible effects on immunity of isoniazid prophylaxis given during primary infection of man. *S. R. M. Bushby*

CROWLE, A. J. & RIEMENSNIDER, D. K. **Lack of Any Antagonism between Pyridoxine and Isoniazid in the Chemotherapy of Acutely or Chronically Tuberculous Mice.** *Tubercle.* 1960, Dec., v. 41, No. 6, 450–53. [23 refs.]

In these experiments groups of mice were infected intravenously with human tubercle bacilli and the effects of treatment were assessed by the closeness of the specific gravity of the lungs of the treated animals to that of those of uninfected mice.

The data of 6 experiments are presented in tabular form. The daily doses of isoniazid were 0·05 and 0·1

mgm. administered by stomach tube, and they were given with and without 0·02, 0·2 or 2 mgm. of pyridoxine [B6]; treatment was started at intervals ranging from 5 to 23 days after infection and its duration was either 9 or 12 days. In none of the experiments was there any evidence that B6 interfered with the antituberculous activity of isoniazid; in fact, in 3 experiments the vitamin appeared to enhance the activity, and in 1 of these experiments in which there was no evidence of 0·1 mgm. isoniazid affording protection when given alone, the addition of 2·0 mgm. B6 gave very definite protection.

Although this failure to demonstrate interference by B6 in experimental tuberculosis is in agreement with the results of most other workers, it is in apparent direct conflict with those of McCune *et al.* [this *Bulletin*, 1958, v. 33, 456]; the experiments of the workers were, however, prolonged and the authors suggest that in the mouse adaptive metabolic changes develop, and therefore such changes should be looked for in man. In the meantime, however, these and other studies indicate that B6 can be used in man with isoniazid without lessening the antituberculous activity. *S. R. M. Bushby*

Andrejew, A., Gernez-Rieux, C. & Tacquet, A. Essais de différenciation des mycobactéries sensibles et résistantes à l'INH à l'aide de tests quantitatifs et qualitatifs de l'activité peroxydasique. Discussion de questions techniques. [**Attempts to differentiate INH-Sensitive and INH-Resistant Mycobacteria by means of Quantitative and Qualitative Tests of Peroxidase Activity**] *Ann. Inst. Pasteur.* 1960, Dec., v. 99, No. 6, 821–38. [15 refs.]

The authors have previously reported [this *Bulletin*, 1957, v. 32, 495; 1959, v. 34, 663] that whereas isoniazid-sensitive tubercle bacilli are peroxidase-positive, both intact and disintegrated isoniazid-resistant variants are peroxidase-negative. In the present paper, the authors first discuss the quantitative methods of measuring peroxidase-activity; they prefer pyrogallol as the hydrogen acceptor because of the stability of its oxidized product and because the reaction is more specific, especially when it is done at *p*H 6.

The authors then describe their experiences with the qualitative test on mycobacteria growing on Löwenstein slopes; for this test they prefer to use benzidine because with it the method is simple and rapid. The results of testing human, bovine and avian tubercle bacilli and atypical mycobacteria with benzidine, pyrogallol and catechol, show that the benzidine test was the most consistent in showing human tubercle bacilli, sensitive to isoniazid, to be peroxidase-positive, and the highly resistant strains to be negative, and avian tubercle bacilli and atypical mycobacteria (groups I, II, III & IV) to be positive; by the catechol test all 24 strains of the latter group were negative.

In the benzidine method, a mixture of equal parts 1% benzidine in normal acetic acid and 1% hydrogen peroxide is poured over the culture and in 2–15 minutes a positive result is shown by the colonies turning blue; a strong solution of peroxide should be used with strongly catalase-positive strains. *S. R. M. Bushby*

Luppi, A. Isolamento di Mycobatteri atipici da latte vaccino naturale. (Descrizione e caratteristiche.) [**Atypical Mycobacteria isolated from Unpasteurized Milk**] *Nuovi Ann. d'Igiene e Microbiol.* 1960, Sept.–Oct., v. 11, No. 5, 409–19. [16 refs.]

In order to learn something about the incidence and the characteristics of atypical mycobacteria isolated from unpasteurized milk in the province of Rovigo, 100 samples of 200 c.c. each were taken from dairies and milk roundsmen and were then homogenized by Roulin's method. Biological tests were performed on guineapigs and cultures made in "IUTM" [not described].

From the 100 samples 8 acid- and alcohol-resistant strains of mycobacteria were isolated which were then tested further for pathogenicity, cord formation, resistance to light, catalase, reduction of colouring agents, and sensitivity to streptomycin, isoniazed, and PAS.

All were scotochromogens, none grew at 47°C., and all more rapidly at 37°C. than at 20°C. All were catalase positive, no cord formation was found, all were positive to neutral red, 4 to Nile blue, and 7 to 2-6-dichlorophenol-indophenol. Tested against the above tuberculostatics at 10 and 200 μgm., growth against isoniazid was notably less than against the other 2, only 1 strain growing abundantly in this, though curiously enough according to the table growth against isoniazid was rather better at 200 μgm. than at 10. 2 strains did not develop on Sauton medium; none belonged to *Nocardia* spp., 1 strain caused the death of a guineapig, and a mouse, and was re-isolated from the former but not from the mouse.

The author points out that a fatty ambient may well protect and even favour the development of virulence of atypical mycobacteria and that they can be present even after pasteurization. The hygienist should therefore exercise caution when such an organism is reported from milk *W. K. Dunscombe*

Lin, Chau-Ching, Tsai, Hsiu-Hwa, Hsu, Shu-Tao & Loo, Min-Chieng. **Studies on the *Corynebacterium diphtheriae* isolated in Taipei.** *J. Formosan Med. Ass.* 1960, May 28, v. 59, No. 5, 281–4, 2 figs. [19 refs.]

"We classified the types of 47 strains of C. diphtheriae isolated from the patients admitted in the Provincial Taipei Hospital and Taipei City Hospital for Infectious Diseases during the epidemic of the winter of 1956–7 as follows: Type Gravis 59·6%, Type Mitis 25·5%, and Type Intermedius 14·9%.

"There were some deaths from each type of C. diphtheriae, and no significant relationship was found between mortality and types of bacilli.

"We found that Elek's medium was convenient for testing the toxin production of C. diphtheriae and had a close correlation to virulence test on animals."

Buddingh, G. J. & Henigst, W. **Experimental Infection of Embryonated Eggs with *Corynebacterium diphtheriae*.** *Amer. J. Path.* 1960, Oct., v. 37, No. 4, 477–95, 1 text fig. & 10 figs. on 2 pls. [12 refs.]

The susceptibility of embryonated chick eggs to graduated doses of diphtheria bacilli has been investigated and

also the establishment of diphtheria infection in such eggs. A definite increase in the LD50 required was observed as the age of the embryo increased. Thus for a 9-day embryo it was found to be 1/115 of a guineapig MLD whereas for the 15-day embryo it was 1/13. In the observations on infection it was found, as had been discovered earlier by GOODPASTURE and ANDERSON, that only recently isolated strains could initiate infection if carefully washed free of preformed toxin.

With a strain which is described as "gravis-like" selected from a local epidemic (Louisiana, 1954), 70 14-day embryos were infected. About 75% perished. A typical pseudo membrane was produced on the surface of the chorio-allantois in most cases and the formation of this was promoted by alternating phases of bacterial growth with accumulation of polymorphonuclear leucocytes followed by their destruction and further growth of bacteria. There was no evidence of invasion of the more remote parts of the embryo but evidence of vascular damage by absorbed toxin.

The outcome of life and death appeared to depend on a fine interplay between the defensive forces and the invading bacteria and to be independent of antitoxin production. There was no evidence that the bacteria isolated from the embryos which survived were less able to produce toxin than those recovered from the embryos which died.

[The authors do not remark on the interesting analogy between their observations on the defective invasive properties of stock strains of all types and those of NIGGEMEYER and others who emphasized that it is only in very recently isolated strains that toxic factors other than the classical lethal toxin can be recognized.]

J. W. McLeod

MASHILOVA, G. M. **Studies of the Oxidative-Reductive Activity of *Corynebacterium diphtheriae*. I. The Dehydrase Activity of Toxigenic and Non-Toxigenic Strains.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 10, 115–21, 1 fig. [Translated from Russian.]

The toxin-producing activities of diphtheria strains were compared with their ability to reduce methylene blue in the presence of suitable substrate in conditions modelled on the Thunberg tube experiment [this *Bulletin*, 1952, v. 27, 889]. Some correlation was demonstrated between dehydrogenase activity so determined and the toxin-producing activity of standard laboratory strains as judged by skin-tests on experimental animals and double diffusion in agar gels against diphtheria antitoxin. There were some exceptions; among recently isolated strains dehydrogenase activity was weak equally with toxigenic and non-toxigenic forms. It would appear, therefore, that the dehydrogenase test performed in this way is a method of assessing the adaptation of the bacterium to growth in artificial conditions of culture rather than to its toxigenic activity.

J. W. McLeod

JOÓ, I. & PUSZTAI, Zsuzsanna. **Interconnexion between the Protective Antigen and the Histamine-Sensitizing Factor of *Bordetella pertussis*.** [Correspondence.] *Nature.* 1960, Oct. 22, v. 188, 331–2. [14 refs.]

An attempt has been made to find the relationship between the histamine sensitizing factor of *Bordetella* [*Haemophilus*] *pertussis* and the antigen responsible for protecting mice against pertussis given by the intracerebral route. Suspensions of pertussis organisms grown on solidified semi-synthetic medium were inactivated either by incubation at 37°C. for 24 hours with 0·3% formalin or by heating to 56°C. for 30 minutes in the presence of 1:5, 000 merthiolate [thiomersal]. It was found that the suspensions treated with merthiolate were significantly superior to those treated with formalin in both their mouse-protective potency and histamine-sensitizing activity. From this and other data the authors have concluded that if the mouse-protective potency and histamine-sensitizing activity are not identical then they are closely related and have a similar chemical structure.

[See also this *Bulletin*, 1959, v. 34, 1048.]

F. T. Perkins

SUGIYAMA, H., DACK, G. M. & LIPPITZ, G. **Agglutinating Antiserum for the Isolation of *Salmonella* with special reference to Isolation from Egg Albumin.** *Applied Microbiol.* Baltimore. 1960, July, v. 8, No. 4, 205–9. [11 refs.]

The use of specific agglutinating sera for concentrating particular micro-organisms in an inoculum from which it is desired to obtain pure cultures is not novel. It has been used experimentally with artificial mixtures but because it has not given very reliable results in routine practice with natural material comparatively little has been published about the method.

This paper describes an improved method for the isolation of salmonella organisms from egg albumin by preliminary incubation for 18 hours at 37°C. in lauryl tryptose broth containing polyvalent salmonella flagellar antiserum and plating the sediment for the isolation of the salmonellae. In comparative tests it was found that the use of the agglutinating serum greatly improved the isolation rates and yet further improvement was obtained if the broth was enriched with selenite-cystine. It is not clear from the paper how far the authors have tried out the method in routine practice.

H. J. Bensted

RUSU, V. *et al.* Considérations sur la valeur de l'association de la lysogénéité de *S. typhi* à la lysotypie directe dans l'étude épidémiologique. [**Considerations concerning the Value of associating the Lysogenicity of *Salm. typhi* with Direct Lysotyping in Epidemiological Investigation**] *Arch. Roumaines Path. Expér. et Microbiol.* 1960, June, v. 19, No. 2, 237–54. [21 refs.]

In a particular area in Rumania where the incidence of typhoid fever is very high it was found that nearly every strain isolated from excreters was untypable by the range of typing phages available up to 1958. In that year the Rumanian institute received from the Central Enteric Reference Laboratory, Colindale, an additional set of 11 typing phages which included phage 38 and it was then found that about half of the previously untypable strains

could be identified as type 38. This phage type proved to be the prevailing one in this highly infected area. Nevertheless there were still large numbers of cultures giving atypical reactions or degraded forms which could not be typed. However by investigating the lysogenicity, and the sensitivity of these strains to lysogenic phages it was possible to obtain patterned reactions which proved to be of considerable epidemiological value.

H. J. Bensted

GAINES, S., CURRIE, J. A. & TULLY, J. G. **Production of Incomplete Vi Antibody in Mice.** *Proc. Soc. Exper. Biol. & Med.* 1960, Aug.–Sept., v. 104, No. 4, 602–5.

This paper produces evidence to show that the type of antibody induced in mice by Vi antigen may vary in accordance with the strain of mice used for experiments. LANDY'S original experiments with purified Vi antigen [this *Bulletin*, 1953, v. 28, 215, 216, 855; 1957, v. 32, 796] and the Swiss Bagg strain of mice showed that this strain responded to the antigen preparation by producing specific antibody which could passively protect against a virulent typhoid bacillus challenge. Similar results were obtained with an inbred variant of the Bagg strain (BALB/c mice), but although another strain (Cinnamon) of mice could be actively protected against a virulent challenge by immunization with the purified Vi antigen, specific Vi haemagglutinin could not be demonstrated in their sera by the saline haemagglutinin test for complete Vi antibody. When, however, the serum dilutions were made in 15% bovine serum albumin the results indicated the presence of an incomplete type of Vi antibody. Absorption tests confirmed the specificity of this incomplete Vi antibody which nevertheless was, in passive protection tests, as protective as the complete Vi antibody elicited in the BALB/c mice.

The determination of Vi antibody in man after antityphoid vaccination, when carried out by either bacterial agglutination or haemagglutination (saline), often fails to show any Vi antibody even when the vaccine contains potent Vi antigen. It is suggested that it might be profitable to examine all sera without demonstrable complete Vi antibody for evidence of incomplete antibody.

H. J. Bensted

GAINES, S., TULLY, J. G. & TIGERTT, W. D. **Studies on Infection and Immunity in Experimental Typhoid Fever. II. Susceptibility of Recovered Animals to Re-Exposure.** *J. Exper. Med.* 1960, Dec. 1, v. 112, No. 6, 1023–36, 6 figs. [17 refs.]

Very young chimpanzees developed typhoid fever when they ingested large numbers of a mouse-virulent Vi strain of the typhoid bacillus [EDSALL *et al.*, this *Bulletin*, 1961, v. 36, 79]. The numbers of organisms required to produce infection with a bacteraemia varied from 4×10^9 to 100×10^9. A year and half after recovery from the disease the animals were re-exposed to infection. The primary infection had been induced in each case by giving the animal a banana into which the desired number of bacteria had been injected and the same method was followed in the re-exposure experiments. The initial infections were with *Salmonella typhi*, strain 2593, whereas strain Ty2 was used for re-exposure; Ty2 is somewhat more virulent than strain 2593. Chimpanzees that had recovered from an infection induced with 100×10^9 *Salm. typhi*, 2593, resisted re-infection with 100×10^9 *Salm. typhi* Ty2 18 months later, but those animals previously infected by ingesting a dose of 4×10^9, strain 2593, were found to be not completely protected against a challenge 18 months later with 87×10^9, strain Ty2. The control animals, challenged by the same method with 100×10^9 *Salm. typhi* Ty2, developed febrile responses, bacteraemia and the other characteristic clinical and laboratory features.

These important experiments indicate that the degree of immunity which recovery from typhoid fever may confer against a second or subsequent infection is only likely to be significant if the primary disease was the result of a very heavy infection. The 2 strains of typhoid bacilli used in these experiments were of different phage types although of approximately the same mouse virulence. It is rather remarkable that where the ingestion of such very large numbers of organisms are required to produce a clinical response the difference between resistance and infection should depend on a difference of the order found between the original and subsequent infecting doses. It is of particular interest to compare these experimental results with the account by MARMION *et al.* [this *Bulletin*, 1953, v. 28, 902] of 2 large outbreaks of typhoid fever in the same community within 5 months in which there were 11 examples of second infections. *H. J. Bensted*

MESROBEANU, Lydia & TEODORESCO, G. Variation du métabolisme microbien, en fonction de la peptone utilisée dans le milieu de culture. L'activité respiratoire, la catalase et les déhydrogénases des variantes "S" et "R" de *Typhi murium*. **[Variations of Microbial Metabolism as related to the Peptone used in the Culture Medium, Respiratory Activity, Catalase and Dehydrogenases of *Salm. typhi-murium*, S and R]** *Arch. Roumaines Path. Expér. et Microbiol.* 1960, Sept., v. 19, No. 3, 355–65, 5 graphs.

Young cultures of smooth strains of *Salmonella typhi-murium* show a higher respiration rate than rough strains up to 8 hours' incubation, but after 22 hours' incubation the rate in rough strains is higher than that of the smooth strain. An acid fibrin hydrolysate medium showed higher respiratory capacity than two other commercial brands of peptone. In general the behaviour of the microbial catalases in relation to enzymatic activity and age of culture was of the same order as the respiratory activity, but the differences between the three types of peptone were not so clear-cut. In studying the activity of the dehydrogenases it was found that the culture medium containing fibrin hydrolysate was the only one in which conclusive results were obtained; whatever its source, after 22 hours' incubation the dehydrogenase activity of the smooth culture was greater than that of rough cultures.

[See also KNOTHE *et al.*, this *Bulletin*, 1958, v. 33, 262, 978.] *H. J. Bensted*

BARON, L. S. & FORMAL, S. B. **Immunization Studies with Living Vaccine of *Salmonella typhimurium*.** *Proc. Soc. Exper. Biol. & Med.* 1960, Aug.–Sept., v. 104, No. 4, 565–7. [16 refs.]

TOPLEY'S classical epidemiological experiments with mouse typhoid showed that killed *Salmonella typhimurium* vaccines gave poor protection to mice exposed to natural infection with mouse typhoid [GREENWOOD *et al.*, this *Bulletin*, 1931, v. 6, 607], but HOBSON [*ibid.*, 1958, v. 33, 164] was able to show that mice, experimentally infected with a relatively avirulent strain of *Salm. typhimurium*, exhibited resistance to a subsequent challenge with a virulent strain.

The present paper is concerned with immunization experiments in mice with living vaccines. The strain of organism used was a double mutant of a virulent strain of *Salm. typhi-murium*; the first process yielded a streptomycin-dependent mutant, which was unstable, and the second a purine-requiring mutant which showed no evidence of reverting to the purine-streptomycin-independent state. There appeared to be no evidence that a living vaccine prepared from this mutant strain offered better protection against experimental infection than the normal heat-killed preparations.

H. J. Bensted

TANAKA, N., NISHIMURA, T., YAMAGUCHI, H. & YOSHIYUKI, T. **Histochemical Studies on Experimental Typhoid by means of Fluorescein-Labelled Antibody. II. Cellular Localization of the Antigens of *Salmonella enteritidis* in the Process of the Infection of Experimental Typhoid.** *Japanese J. Microbiol.* 1960, Jan., v. 4, No. 1, 35–41, 7 figs. (6 on pl.)

This paper describes the cellular localization of the antigens of a mouse-virulent strain of *Salmonella enteritidis* after intraperitoneal and intravenous injection into mice by employing the indirect layering method with antiglobulin labelled with fluorescein isothiocyanate. The appearance, on the 3rd day after the intraperitoneal injection of 10^{-8} mgm. of the bacilli, of the bacterial antigens in the liver and spleen, and development of the granulomata, are described. It is suggested that the granulomata may be formed by the antigen-antibody reaction. The amount of bacterial antigens which appeared to be present by this technique corresponded reasonably well with the number of organisms recovered by cultural methods. Conventional staining techniques did not show up the bacterial antigens in the form of rods whereas the fluorescent-antibody method employed demonstrated the rod-shaped bacterial antigens very clearly in the tissues.

[For part I, see this *Bulletin*, 1961, v. 36, 80.]

H. J. Bensted

FULTON, M., SZAFRAN, Philomena & LESKO, M. M. **Five Less-Common *Salmonella* Serotypes from Congo Reptiles.** [Correspondence.] *Nature.* 1961, Jan. 21, v. 189, 240–41.

STOCKER, B. A. D., MCDONOUGH, M. W. & AMBLER, R. P. **A Gene determining Presence or Absence of ε-N-Methyl-Lysine in Salmonella Flagellar Protein.** *Nature.* 1961, Feb. 18, v. 189, 556–8.

HUET, M. & BONNEFOUS, Solange. Essai d'un milieu de transport et de conservation des selles pour l'isolement de *Salmonella* et *Shigella* par coprocultures. **[Trials of a Medium for the Transport and Preservation of Stools for Isolation of *Salmonella* and *Shigella*]** *Arch. Inst. Pasteur de Tunis.* 1960, Mar., v. 37, No. 1, 37–47, 1 graph.

The "transport medium" used by these authors was that of HAJNA (*Pub. Health Lab.*, 1955, v. 13, 59). This fluid has a long formula and contains in addition to citrate-phosphate buffer and glycerol, sodium desoxycholate and yeast extract. The specimens tested were faecal samples from suspect carriers of Salmonella Tunis and dysentery patients. It is difficult to follow exactly the technique used, but it would appear that each specimen was examined blindly and the result of the cultural examination recorded as positive or negative for salmonellae or shigellae as the case might be. Although it was clear that the survival of the pathogenic members of the enterobacteriaceae depended on the temperature at which the mixture of faeces and transport medium was stored, there were other factors of almost equal importance which were not investigated in the present study. [For instance, IDINA [this *Bulletin*, 1961, v. 36, 192] in quantitative determinations of viable shigellae in naturally infected faeces, stored without any added preservative, showed that initial bacterial counts of *Shigella flexneri* or *Sh. sonnei* in faeces stored at −12°C. were maintained for long periods and viable organisms were still present at the end of of 2 months whereas a representative portion of the same specimen stored under the same conditions at 37°C. failed to show survivors after about 6 days. At other temperatures this same author found, particularly at so-called room temperatures, the survival rates to be very variable.

While there seems to be little doubt about the value of the original buffered glycerol-saline of SACHS [*ibid.*, 1940, v. 15, 135] for the preservation of faecal specimens for the isolation of enteric pathogens it is a little difficult to understand the particular argument the authors wish to present.]

H. J. Bensted

SHIPE, E. L., Jr., FIELDS, Adelaide & SHEA, Janice R. **Comparison of Three Preservatives for Bacterial Enteric Pathogens in Fecal Specimens.** *Pub. Health Lab.* 1960, Sept., v. 18, No. 5, 95–103.

The 3 fluids which were compared as preservatives for enteric pathogens were SACHS buffered glycerol-saline [this *Bulletin*, 1940, v. 15, 135], HAJNA specimen preservative (constitution not disclosed) and disodium ethylenediamine tetra-acetate (EDTA).

The tests were carried out with artificial mixtures by adding broth cultures of various pathogens (10 *Shigella*, 3 Vi strains of *Salmonella typhi* and 3 strains of other salmonellae) to samples of faeces free of pathogens but

containing known concentrations of non-pathogenic faecal bacteria. Each test sample was then divided into 3 parts and mixed with the preserving fluids and stored for periods of 1 and 4 days at 25°C. and then assayed by plating on bismuth sulphite agar, SS agar, brilliant green agar and also MacConkey's agar.

The EDTA preservative was found to give about the same recovery rate as the other two fluids for salmonellae up to 1 day but, with SS agar for plating, the 4-day tests showed the EDTA to be superior. This advantage was more marked in the case of the shigellae.

H. J. Bensted

SHIPE, E. L., Jr., FIELDS, Adelaide & SHEA, Janice R. **Effect of Disodium Ethylenediamine Tetraacetate and Glycerol on Survival of Shigellae and Normal Fecal Flora.** *Pub. Health Lab.* 1960, Sept., v. 18, No. 5, 104–10.

The work reported here is a continuation of that described in the previous abstract. In place of EDTA alone, the effect of various combinations of EDTA with glycerol-saline with controlled *p*H to enhance the survival rates of shigella organisms in the presence of sterile faeces was studied, and the results were compared with those obtained with buffered glycerol-saline and HAJNA specimen preservative. The methods used were similar to those employed for the previous study.

One particular combination of EDTA and glycerol-saline at *p*H 5·5 was found to give a recovery rate of 45% of shigellae after 4 days at 25°C. as compared with 2 and 3% respectively for buffered glycerol-saline and specimen preservative.

[While the results reported may be accepted under the conditions of the experiments described, it cannot be assumed that under natural conditions results of the same order would be obtained. The survival of shigellae in natural exudates, with or without preservatives, can vary very widely and it is considered that more extensive experience of the proposed preservative would be desirable before making recommendations.]

H. J. Bensted

STENZEL, W. Zur Kenntnis der *Shigella boydii* 11. [**The Study of *Shigella boydii* 11**] *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 146, No. 5, 450–57. [12 refs.]

The strain, designated A 316 XIA, was obtained from a patient evacuated from Egypt suffering from dysentery. The exact relationship of the strain to the patient's illness is uncertain as *Entamoeba histolytica* was also present in the stool. The strain was found to diverge in some particulars, especially inability to ferment mannite, from the classical Boyd 11 strains, and on proceeding to antigenic analysis it was found that although the serum obtained by injecting this strain into animals corresponded closely in its activity to the sera obtained with the classical Boyd 11 strain, suspensions of A 316 were not able to exhaust the sera appropriate to the classical strains although suspensions of the latter completely exhausted the agglutinins of the sera prepared with the new strain.

The conclusion is drawn that this is a strain of the Boyd 11 group defective in an antigen component present in the classical strains. It is suggested that it should be described as Serotype A 316 XIA.

The strongest evidence for the pathogenic significance of this bacterium which the author can produce is that it gives a definitely positive reaction in Bingel's guineapig bladder test. He has shown that the dysentery bacteria set up incontinence of urine, oedema of the perineal tissue and sub-serosal haemorrhages in the guineapig bladder in a much greater degree than any of the other enterobacteriaceae.

(BINGEL, *Ztschr. f. Hyg. u. Infektionskr.*, 1944, v. 125, 110, 574, 610.) *J. W. McLeod*

NELSON, J. D. & WHITAKER, Jo Anne, with the technical assistance of B. HEMPSTEAD. **Diagnosis of Enteropathogenic *E. coli* Diarrhea by Fluorescein-Labeled Antibodies.** *J. Pediatrics.* St. Louis. 1960, Nov., v. 57, No. 5, 684–8.

This paper is concerned with the application of the fluorescent-antibody technique to the direct examination of faecal smears obtained from patients suffering from infantile diarrhoea. Preliminary screening tests are undertaken with fluorescein isothiocyanate labelled with pooled globulin fractions of the various type antisera, and those specimens showing positive staining are re-examined as a duplicate series of smears stained with individual type sera, globulin fractions, conjugated with fluorescein. In comparative tests with conventional bacteriological methods the fluorescent-antibody technique came out very well. It is claimed that the method is very rapid and reliable. Moreover the results are not influenced by antibiotic therapy, or by the presence of other pathogenic or non-pathogenic organisms in the smear [this would surely depend on the antigenic relationship of the organisms concerned] and it is also suggested that the test is particularly valuable for the identification of particular serotypes of the enteropathogenic *E. coli* when they are present in small numbers and likely to be overgrown by other bacteria when examined by normal bacteriological methods. These are high claims and although the wider application of the fluorescent-antibody is very attractive a certain amount of reserve seems desirable until deeper experience is available.

H. J. Bensted

ADLER, H. I. & HASKINS, Sara D. **Heterogeneity of Cultures of *Escherichia coli B/r.*** [Correspondence.] *Nature.* 1960, Oct. 15, v. 188, 249–51, 1 fig.

Escherichia coli B has been maintained for many years by laboratories interested in bacteriophage synthesis and behaviour, and this particular strain is peculiarly sensitive to the T series of coliphages. *E. coli* B/r is a mutant of the parent strain selected after irradiation with ultraviolet light. This mutant is characterized by its high resistance to UV light, X-rays, penicillin and sodium sulphathiazole. The snake-like forms, so frequently found in B cultures after UV irradiation, are only occasionally found in B/r cultures.

The object of this communication is to draw attention

to the results of a comparison, under standardized conditions, of strains of *E. coli* B/r obtained from different sources, which disclosed variations in sensitivity to the different agents used: UV light, X-rays and penicillin. These changes do not constitute reversion to parent characteristics but the cultures showed lowered resistance to UV irradiation as compared with the original B/r. These differences in sensitivity to UV light and X-rays depend upon the growth medium used and other factors. and this observed heterogeneity in the B/r strains examined indicates the need to ensure that the actual strain used in radiation bacteriological research conforms in all respects with the original culture of *E. coli* B/r.

H. J. Bensted

STAPLETON, G. E. & ENGEL, M. S. **Cultural Conditions as Determinants of Sensitivity of *Escherichia coli* to Damaging Agents.** *J. Bacteriology.* 1960, Oct., v. 80, No. 4, 544–51, 4 figs. [20 refs.]

The sensitivity of certain strains of *Escherichia coli* to inactivation by X-rays can be modified by alterations in the constitution of the culture medium in which the bacterial cells are grown. It does not seem very clear exactly how the resistance to UV light and to X-rays of *E. coli*, strain B/r, can be adequately controlled or standardized so long as the culture is normally grown in nutrient broth since the exact standardization of such a culture medium is hardly possible. The authors show, however, that a particular culture of *E. coli* B/r grown aerobically under different conditions but subjected to exactly the same irradiating dose of X-rays have different survival curves. It should be mentioned that the B/r strain is a resistant mutant of *E. coli* B which is sensitive to UV light and generally well known for its sensitivity to the T system of coliphages. The parent strain appears to be reasonably stable in respect to its sensitivity to damaging agents whereas the resistant mutant, while not showing signs of complete reversion when subjected to abnormal environments, does not display the same stability as that exhibited by its parent. [See also ADLER and HASKINS, above.]

H. J. Bensted

CARO, L. G., VAN TUBERGEN, R. P. & FORRO, F., Jr. **The Localization of Deoxyribonucleic Acid in *Escherichia coli*.** *J. Biophysic. & Biochem. Cytol.* New York. 1958, July 25, v. 4, No. 4, 491–4, 2 text figs. & 2 figs. on pl. [11 refs.]

HOLMES, R., SHEININ, Rose & CROCKER, B. F. **A Study of the Permeability Barrier to β-Galactosides in *Escherichia coli* B.** *Canadian J. Biochem. & Physiol.* 1961, Jan., v. 39, No. 1, 45–54, 5 figs. [22 refs.]

SHEININ, Rose & CROCKER, B. F. **The α-Galactosidase Activity of *Escherichia coli* B.** *Canadian J. Biochem. & Physiol.* 1961, Jan., v. 39, No. 1, 55–61, 4 figs. [19 refs.]

SHEININ, Rose & CROCKER, B. F. **The Induced Concurrent Formation of α-Galactosidase and β-Galactosidase in *Escherichia coli* B.** *Canadian J. Biochem. & Physiol.* 1961, Jan., v. 39, No. 1, 63–72, 11 figs. [28 refs.]

ROWBURY, R. J. & WOODS, D. D. **Further Studies on the Repression of Methionine Synthesis in *Escherichia coli*.** *J. General Microbiol.* 1961, Jan., v. 24, No. 1, 129–44, 6 figs. [21 refs.]

GIBBS, M. & PAEGE, L. M. **The Anaerobic Dissimilation of D-Xylose-1-C^{14}, D-Arabinose-1-C^{14}, and L-Arabinose-1-C^{14} by *Escherichia coli*.** *J. Biol. Chem.* 1961, Jan., v. 236, No. 1, 6–9. [24 refs.]

JÄNNES, J. & SARIS, N. E. **Effect of 4-Deoxypyridoxine on Tryptophan Metabolism in *Escherichia coli*.** *Ann. Med. Exper. et Biol. Fenniae.* Helsinki. 1960, v. 38, No. 4, 442–6, 1 fig.

CHALOUPKA, J. **Localization of a Protease in the Cell of *Escherichia coli*.** [Correspondence.] *Nature.* 1961, Feb. 11, v. 189, 512, 1 fig.

HAGER, L. P. & KORNBERG, H. L. **On the Mechanism of α-Oxoglutarate Oxidation in *Escherichia coli*.** *Biochem. J.* 1961, Jan., v. 78, No. 1, 194–8, 3 figs. [16 refs.]

IENIŞTEA, C., DUMITRIU, S. & MAIOR, O. Cercetarea prezenţei histidindecarboxilazei la tulpini de *Escherichia coli*. **[Investigations on the Presence of Histidin Decarboxylase in *Escherichia coli* Strains]** *Microbiol., Parazitol., Epidemiol.* Bucharest. 1960, Nov.-Dec., v. 5, No. 6, 523–9, 1 fig. English summary.

HILL, Ruth F. & SIMSON, Eva. **A Study of Radiosensitive and Radioresistant Mutants of *Escherichia coli* Strain B.** *J. General Microbiol.* 1961, Jan., v. 24, No. 1, 1–14, 3 figs. [29 refs.]

RENOUX, G. Nouvelles épreuves bactériostatiques pour différencier les *Brucella*. Résultats et conséquences. **[New Bacteriostatic Tests for Differentiating *Brucella* Organisms]** *Arch. Inst. Pasteur de Tunis.* 1960, Mar., v. 37, No. 1, 23–35.

This paper is concerned with a new method of classifying *Brucella* organisms in accordance with their sensitivity to the inhibitory action of methylene blue (1:120,000), Janus green (1:80,000) and erythromycin (15 μgm./ml.). This method would enable 8 different reaction groups to be recognized, but it can be simplified by using only Janus green and erythromycin. The 4 groups offer classification

of the great majority of smooth cultures of the brucellae; it is claimed that 1086 such strains readily fell into one of the 4 groups and that the results were reliable and reproducible. *H. J. Bensted*

KOROBKOVA, Y. I. & PAVLOVA, L. P. **Lysogeny in a Subculture of Plague Vaccine Strain EV (Girard and Robic).** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 3, 321–6, 8 figs. on 2 pls.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 583.]

BURDON, K. L. & WENDE, R. D. **On the Differentiation of Anthrax Bacilli from *Bacillus cereus*.** *J. Infect. Dis.* 1960, Sept.–Oct., v. 107, No. 2, 224–34, 2 figs. [23 refs.]

The most important point made in this communication is that when erroneous observations due to the use of mixed cultures containing a minority of anthrax spores have been discarded, there is still evidence that *Bacillus cereus* is endowed with pathogenic activity. This can be elicited by passing a culture in rapid succession through blood-containing media. The injection of considerable doses of suspension from the last of the series of cultures frequently causes death of mice with invasion of the bloodstream, and a deep ulceration of the skin may be caused by subcutaneous inoculation [this *Bulletin*, 1958, v. 33, 991].

Such strains are differentiated from *B. anthracis* in the following respects: (1) they do not produce capsules in the animal body; (2) mice are not protected by previous anthrax immunization; (3) they are not susceptible to the gamma phage which attacks anthrax bacilli; (4) smooth colonies and capsuled forms are not reproduced on media of reinforced Na bicarbonate content; (5) they grow, with rare exceptions, on 10% penicillin agar.

[See also this *Bulletin*, 1956, v. 31, 953.]

J. W. McLeod

SEBALD, M. & PRÉVOT, A. R. Étude qualitative et quantitative du pouvoir lipidolytique de 86 souches de *Clostridium* anaérobies. [**Qualitative and Quantitative Study of the Lipolytic Capacity of 86 Strains of Anaerobic *Clostridium***] *Ann. Inst. Pasteur.* 1960, Sept., v. 99, No. 3, 386–400, 3 figs. [19 refs.]

The authors describe a new technique for demonstrating the lipolytic activity of anaerobes. This consists in growing the organisms in the presence of the 3 Tweens, 40, 60 and 80. These are polyesters of sorbitol with palmitate, stearate and oleate respectively. The medium used is a slight modification of that of SIERRA [this *Bulletin*, 1957, v. 32, 885] and consists of 1% peptone, 0·5% sodium chloride in a soft agar which also contains 0·01% calcium chloride, and 0·5% of the Tween under investigation. The most actively lipolytic clostridia give positive results with all 3 Tweens; the less active with 40 and 60 but not with 80. The actively lipolytic colonies growing in such media are surrounded by haloes of the precipitated calcium salts of the fatty acids. These have characteristic appearances which are illustrated as magnified at 1,040. A positive can be recognized by macroscopic appearance where it is pronounced and by the microscope where it is slight.

A list of the reactions obtained with 86 strains of anaerobe are given. Those outstanding in their capacity are *Clostridium botulinum*, especially type A and B, *Cl. sporogenes* and some allied forms. The *Cl. oedematiens* and *Cl. histolyticum* have given negative results. A weak aspect of such observations is the failure of a number of varieties such as *Cl. chauvoei* and *Cl. gigas* to grow in the medium. The observations have been supplemented by testing the effect of culture filtrates incorporated in cupped plates containing medium and Tween. In a general way these observations confirm the results obtained by the direct cultural method and shows that the enzymes are, for the most part, constitutive. Evidence of adaptive enzyme, however, was obtained in the case of *Cl. welchii*, and with one strain of *Cl. oedematiens* a positive was obtained with culture filtrate notwithstanding the negative results on the direct culture. The positive results of the diffusing filtrate can be obtained with cultures in simple media like peptone-water but not in the more complex media particularly suitable for the growth of anaerobes such as VF.

J. W. McLeod

GONZALEZ, C. & SIERRA, G. **Lipolytic Activity of some Anaerobic Bacteria.** [Correspondence.] *Nature.* 1961, Feb. 18, v. 189, 601–2.

CRISLEY, F. D. **Routine Method for the Goldfish Assay of Toxin in Crude Culture Centrifugates of *Clostridium botulinum* Type A.** *Applied Microbiol.* Baltimore. 1960, Sept., v. 8, No. 5, 282–5. [11 refs.]

200–250 common goldfish, *Carassius auratus*, 2–3 inches in length and 2–4 gm. in weight, were kept in heavily aerated 30-gallon tanks of aged tap water [this *Bulletin*, 1953, v. 28, 665]. Unaerated 3-gallon "dilution" tanks, 40% full with water at 30°C. were used at room temperature to hold 5 fish injected with a single dilution dose of toxin. The assay fish were acclimatized before use in a separate aerated 30-gallon tank in which the temperature of the water was raised 3°C. every 24 hours; ½-pint of water from the stock tank was added to the experimental tanks 1 hour before they received the infected fish.

A highly toxigenic Hall strain of *Clostridium botulinum* type A was grown in buffered or unbuffered medium [*ibid.*, 1957, v. 32, 1109], and 3 serial transfers at 24-hour intervals were made before inoculating the same medium with approximately 22 million per ml. of washed cells for toxin production.

Pools of equal aliquots from each of 3 50-ml. cultures were centrifuged and refrigerated. Dilutions were made in the buffered medium containing 0·2% gelatine and were kept at 1°C. during the assay. Each group of 5 fish injected with a single dilution were observed for 96–120 hours after receiving the toxic dose; they were fed daily.

The 50% mortality doses were calculated (Reed and Muench) at the end of 36 hours and after deaths from botulism had ceased; death rarely occurred after 72 hours. Expressed as logarithms of the concentration at 72 hours after injection, the LD50 doses showed a mean value of 4·4 with a standard deviation of about 0·30 logarithm units. Control fish injected with type A antitoxin survived lethal dilutions of 10^{-2} and 10^{-3}. A 10^{-1} dilution killed a few protected fish.

Details are given for the maintenance of a healthy stock of goldfish. *Betty C. Hobbs*

Bulatova, T. I. & Kabanova, Y. A. **Identification of the Botulinism Pathogen with Luminescent Sera.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1960, v. 31, No. 3, 403–8, 1 fig. [Translated from Russian.]

Three series of luminescent sera were prepared from the globulin fraction of antibotulinum serum type B by the method of Coons and Kaplan [this *Bulletin*, 1950, v. 25, 730]; isomer II of fluorescein isocyanate was used for labelling. The luminescent sera were precipitated with ammonium sulphate, adsorbed with dried and powdered mouse liver and filtered through an asbestos pad.

Anaerobes tested included strains of *Clostridium botulinum*, types A, B, C, D and E, *Cl. perfringens* [*welchii*], types A, B, C, D and F, *Cl. sporogenes*, *B. anthracoides* and *Bact. coli communis* [*Escherichia coli*].

Luminescence was demonstrated with all strains of *Cl. botulinium*, types A and B, but not with types C, D and E, also with 3/17 strains of *Cl. sporogenes*; an occasional cell and spore showed luminescence in 12 other strains of *Cl. sporogenes*. Agglutination tests showed that the luminescence of *Cl. botulinum* type A and *Cl. sporogenes* was due to antigenic affinity between these strains and *Cl. botulinum* type B.

Adsorption tests were unsatisfactory.

The method is recommended as being highly sensitive, rapid and fairly specific for the identification of *Cl. botulinum* in microscopic preparations. *Betty C. Hobbs*

Sinitsyn, V. A. **Use of the Indirect Haemagglutination Reaction in Detection of Botulinic Toxins. Report 1. Detection of Botulinic Toxins Types A and B by means of the Indirect Haemagglutination Reaction as modified by Rytsai.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1960, v. 31, No. 3, 408–14, 2 figs. [Translated from Russian.]

The indirect haemagglutination test, with the modified method described by Rytsai (*Bull. Acad. Polonaise des Sci.*, Warsaw, 1956, v. 4, 335) was more sensitive than the biological test on white mice for differentiating between the antitoxins of *Clostridium botulinum* types A and B; results could be obtained in 3½–4 hours at 37°C.; maximum sensitivity was obtained at *p*H 6·4–7·0. The determination of unknown concentrations of botulinum toxin required sensitization of the sheep erythrocytes, already treated with tannic acid, with varying doses of antibotulinum serum. *Betty C. Hobbs*

Meisel, H., Albrycht, H. & Rymkiewicz, D. **Comparative Investigations on Toxin, Epsilon Protoxin and Phospholipase C (Alpha Toxin) Content in Culture Fluids, Vegetative Cells and Spores of *Clostridium perfringens* Type *D*.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1960, v. 8, No. 9, 395–400.

Two strains of *Clostridium perfringens* [*welchii*] type D were used (No. 6509 from NIH Bethesda, U.S.A. and No. 1184 Wellcome Research Laboratories, Beckenham, England). Vegetative cells were obtained in beef infusion broth plus glucose and spores in Ellner's medium. (*J. Bact.*, 1956, v. 71, 495).

Phospholipase C, although it had been demonstrated in fluids from VF medium (Weinberg's beef and liver medium), was not found in broth culture fluids; it was found in extracts of vegetative cells at early periods of incubation, but at later stages of growth the enzyme disappeared. Traces of the enzyme were found in extracts of the spores in contrast to the extracts from type A spores which contained large amounts of alpha toxin.

Active epsilon toxin was found in small amounts in type D culture fluids and in cell extracts at early stages of incubation; it was not found in spores. A specific protoxin, activated with trypsin and neutralized by epsilon antitoxin was found in culture fluids, extracts of vegetative cells and spores of type D strains. [see *Bull. Acad. Polonaise des Sci.* Warsaw Sér. Sci. Biol., 1959, v. 7, 395; this *Bulletin*, 1960, v. 35, (196); 1959, v. 34, 1291]. *Betty C. Hobbs*

Guillaumie, Maylis, Kréguer, A., Geoffroy, M. & Ventre, F. Sérums antigangréneux. Persistance de l'immunité anti-*septicum* et anti-*oedematiens* après l'arrêt de l'immunisation correspondante. [**Persistence of Immunity to *Cl. septicum* and *Cl. oedematiens* after Cessation of the Appropriate Immunization**] *Rev. d'Immunologie.* 1960, Oct.–Dec., v. 24, Nos. 5/6, 581–605, 3 figs. [17 refs.]

A study has been made of the response of horses to the successive injection of different anaerobic toxoids. The result of this has been to show that there is a considerable affinity between the alpha toxin of *Clostridium histolyticum* and the active toxin of *Cl. septicum, i.e.* the antibody titre of the serum of horses which have been given a preliminary immunization with *Cl. histolyticum* toxoid some years previously can be markedly raised in its *Cl. histolyticum* antitoxin content by the administration of a small dose of *Cl. septicum* toxoid. This occurs independently by any movement in the anti-collagenase beta titre and a similar rise of the antitoxin for *Cl. septicum* can be obtained if the order of giving the toxins is reversed. No corresponding result is obtained, however, where a *Cl. oedematiens* toxoid is given after the injection of *Cl. septicum* toxoid.

Attention is also drawn to the remarkable persistence of significant titres of antibody to *Cl. oedematiens* toxoids in the sera of horses which have been heavily immunized with such toxoid. It may persist for 6 years.

From observations on the neutralizing powers of the mixed anti-*Cl. septicum* and *Cl. histolyticum* sera at

different intervals after immunization, it is assumed that they contain antibodies specific to *Cl. histolyticum* and *Cl. septicum* toxins and also antitoxin capable of combining with either. *J. W. McLeod*

ŠEBEK, Z. Izolace leptospir ze skupiny *Australis* v českých zemích. [**Isolation of Leptospirae of the Group *australis* in Bohemia**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1961, v. 10, No. 1, 68–72. English summary.

NETER, E., ANZAI, H. & GORZYNSKI, E. A. **Identification of an Antigen Common to *Listeria monocytogenes* and Other Bacteria.** *Proc. Soc. Exper. Biol. & Med.* 1960, Oct., v. 105, No. 1, 131–4. [11 refs.]

Listeria monocytogenes produces a soluble antigen which survives heating at 100°C. for 15 minutes and is readily adsorbed onto the surface of human erythrocytes so that its presence in culture filtrates can be demonstrated by agglutination of antigen-coated red cells by specific anti-*Listeria* sera. The same antigen is present in culture filtrates of *Staphylococcus aureus* and *Bacillus subtilis* and specific anti-*Staphylococcus* sera show high-titre agglutination of erythrocytes coated with antigen derived from all 3 species. The authors discuss the significance of this heterogenetic antigen—antibodies to which are often found in human serum—in relation to the serological diagnosis of listeriosis. *John R. Norris*

NICOLLE, P., GALLUT, J. & LE MINOR, L., with the technical collaboration of P. DUCREST, G. BRAULT & J. QUINIOU. Étude lysogénique, lysotypique, sérologique et biochimique (Cholera-roth et recherche de la lysine décarboxylase) d'une collection de vibrions cholériques et de vibrions El-Tor. [**Lysogenic, Phage-Typing, Serological and Biochemical Studies (Cholera-Red and Demonstration of Lysine-Decarboxylase) on Various Cholera and El-Tor Vibrios**] *Ann. Inst. Pasteur.* 1960, Nov., v. 99, No. 5, 664–71.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1961, v. 58, 584.]

BACTERIOPHAGES

NAKATA, A., SEKIGUCHI, M. & KAWAMATA, J. **Inhibition of Multiplication of Bacteriophage by Actinomycin.** [Correspondence.] *Nature.* 1961, Jan. 21, v. 189, 246–7.

Actinomycin S does not inhibit the growth of *Escherichia coli* B. However, when the antibiotic was added to the culture medium either 5 minutes before or after infection of *E. coli* B with T2r, the number of infective phage particles produced decreased with increasing concentration of actinomycin.

Actinomycin has been reported by KAWAMATA and IMANISHI (*Nature,* 1960, v. 187, 1112) to form a complex with DNA but not with RNA. Phage lysates obtained from cells infected in the presence of actinomycin contained the same amount of DNA as control lysates, but the DNA appeared to be free and not contained within the phage particles since it was destroyed by DNase, was not precipitated by phage antiserum and did not sediment with the phage particles on centrifugation. It is concluded that, like proflavine, actinomycin blocks some final step in phage maturation. *Janice Taverne*

BERTANI, L. Elizabeth. **Host-Dependent Induction of Phage Mutants and Lysogenization.** *Virology.* New York. 1960, Dec., v. 12, No. 4, 553–69, 4 figs. [15 refs.]

Phage P2 grows equally well in *Escherichia coli* C and *Shigella dysenteriae* Sh. When the bacterial strains were irradiated with UV light before infection with irradiated phage, more plaques were formed on strain C than on strain Sh. In addition, more clear plaque type mutants were found among irradiated phage survivors multiplying in irradiated strain C than in irradiated strain Sh or in unirradiated cells. It is generally thought that the reactivation of irradiated phage by UV-irradiated host cells, as well as the increase in the number of mutants among the progeny arising from this reactivation, result from some interaction or recombination occurring between the genetic material of the phage and related material in the host. It appears likely, therefore, that strain C has more genetic material related to phage P2 than has strain Sh.

98 of the clear plaque mutants were tested for their ability to establish lysogeny in the 2 bacterial strains, and they were also examined to see if they would co-operate in lysogenization. [When the frequency of lysogenization of a bacterium is higher after mixed infection with 2 genotypically different phage particles than after infection by 1 only, the phages are said to co-operate in lysogenization, [KAISER, this *Bulletin,* 1957, v. 32, 694 and LEVINE, *ibid.,* 693].] The mutants fell into 3 groups: (A) those which did not lysogenize either strain C or Sh, (B) those which gave clear plaques on Sh but were able to lysogenize strain C, and (C) those which could lysogenize both strains. No evidence of cooperation was obtained upon mixed infection of strain C with any combination of mutants. With strain Sh, cooperation occurred after mixed infection with A and B mutants, and with B and C mutants but not with A and C mutants. *Janice Taverne*

SMITH, J. & WHITE, A. **Effect of Human Sera on the Propagation of Staphylococcal Bacteriophages.** *J. Bacteriology.* 1960, Dec., v. 80, No. 6, 741–3.

When strains of *Staphylococcus aureus* used for propagating phages 52a and 81 were grown in a medium containing human serum and were then infected with their respective phages, the multiplication of the phages was inhibited. At a concentration of 40%, 6 out of 7 samples of serum completely inhibited the growth of phage 52a and 3 out of 7 inhibited phage 81. Sera from patients with infections caused by phage type 81 *Staph. aureus*, or sera from nasal carriers were not more active against phage 81 than other sera. Phage adsorption was not prevented by serum. Heating the serum at 56°C. for 60 minutes did not reduce its effect, nor did incubating it with bacteria before adding phage. Incubating phage in serum for up to 24 hours before mixing it with bacteria did not reduce the number of plaques more than did incubation in broth. Fractionation of serum with ammonium sulphate indicated that the most active fraction was that containing gamma globulin.

Thus although serum did not neutralize the phages or prevent their adsorption, and although it did not interfere with the growth of the host cell, it acted on the cell to prevent phage multiplication after adsorption had occurred. *Janice Taverne*

SASAKI, M. **[Studies on Mycobacteriophages]** *Igaku Kenkyu.* Fukuoka. 1960, Dec., v. 30, No. 12, 3523–39, 4 figs. on 2 pls. [29 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"Several strains of mycobacteria were isolated from soil and three of the strains were proved to be lysogenic. The existence of lysogenic mycobacteria in soil and the origin of mycobacteriophages isolated from soil are discussed. Susceptibility of the various mycobacteria to the temperate phages released by the lysogenic strains, plaque morphology, results of cross resistance tests and electron-microscopic findings are presented. These indicate that these three strains are closely related to each other. Tests on transduction of streptomycin-resistance using one of the phages (R3-A) were not successful.

"Identification and typing of atypical mycobacteria using phages were attempted, but it was not possible to obtain satisfactory results. Attempts to classify phages that show lytic activity to atypical mycobacteria were made by neutralization tests using anti-phage serum. It was found that the host range of the phages varied considerably even in serologically related phages.

"Fundamental conditions necessary for phage susceptibility tests of atypical and saprophytic mycobacteria were examined and discussed."

DREXLER, H. & CHRISTENSEN, J. R. **Genetic Crosses between Restricted and Unrestricted Phage T1 in Lysogenic and Nonlysogenic Hosts.** *Virology.* New York. 1961, Jan., v. 13, No. 1, 31–9, 2 figs. [15 refs.]

EDGAR, R. S. **High Negative Interference and Heterozygosis: a Study of the Mechanism of Recombination in Bacteriophage T4.** *Virology.* New York. 1961, Jan., v. 13, No. 1, 1–12, 3 figs. [20 refs.]

BAUTZ-FREESE, Elisabeth & FREESE, E. **Induction of Reverse Mutations and Cross Reactivation of Nitrous Acid-Treated Phage T4.** *Virology.* New York. 1961, Jan., v. 13, No. 1, 19–30, 9 figs. [17 refs.]

CHRISTENSEN, J. R. **On the Process of Host-Controlled Modification of Bacteriophage.** *Virology.* New York. 1961, Jan., v. 13, No. 1, 40–43.

GROMAN, N. B. & SUZUKI, G. **The Mechanism of Inhibition of Lambda Phage Production at Elevated Temperatures.** *Virology.* New York. 1961, Jan., v. 13, No. 1, 144–6, 1 fig.

STAHL, F. W., CRASEMANN, Jean M., OKUN, L., FOX, Evelyn & LAIRD, C. **Radiation-Sensitivity of Bacteriophage Containing 5-Bromodeoxyuridine.** *Virology.* New York. 1961, Jan., v. 13, No. 1, 98–104, 6 figs. [11 refs.]

VIRUSES

The order in this section is:—**General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Reovirus group; Enteric group; Arthropod-borne group; Others.**

MONTES DE OCA, H., SCHAJOWICZ, F., CABRINI, R. L., FALCOFF, E. & EPSTEIN, B. Multiplicación de diferentes virus en cultivo de tejidos de una nueva cepa celular T9 (CNEA). **[Multiplication of Certain Viruses in Cultures of a New Line of Cells (T9, CNEA)]** *Semana Méd.* 1960, July 25, v. 117, No. 8, 279–83, 10 figs.

The authors have obtained a new continuous line of human cells (T9) derived from an undifferentiated reticulosarcoma which has been carried through 57 passages in medium containing lactalbumin hydrolysate and horse serum. The cells originally had the appearance of fibroblasts, but after 52 days of growth, islands of epithelioid cells appeared which increased in numbers in successive

passages until they became the sole type of cell present. The cells supported the multiplication of western equine encephalomyelitis and the 3 types of poliomyelitis virus, and were suitable for the primary isolation of the latter and its identification by means of neutralization tests.

D. J. Bauer

BUCKLAND, F. E. **Inactivation of Virus Haemagglutinins by *para*-Chloromercuribenzoic Acid.** [Correspondence.] *Nature.* 1960, Nov. 26, v. 188, 768.

The effect of parachloromercuribenzoic acid on the haemagglutinin of a variety of viruses representing the myxo-, adeno-, entero- (including Theiler's GDVII as an enterovirus), reo-, arbor and EMC virus groups was investigated. The substance was tested at 10^{-3} and 10^{-4} M and had no direct effect on red cell receptors. In general the results showed that myxo- and arbor virus (only West Nile and Semliki Forest were tested) haemagglutinins were unaffected whereas reo-, entero- and EMC virus haemagglutinins were destroyed by this substance. The results obtained with adenoviruses enjoin caution in ascribing too much importance to these differences between virus groups, for type 9 and SV 17 (a simian adenovirus) were unaffected whereas the haemagglutinin of type 7 was affected. The activity of the substance against virus infectivity does not correlate with its action against haemagglutinin. Thus GDVII haemagglutinin is destroyed but infectivity remains unchanged whereas the opposite happens for some myxoviruses.

A. J. Beale

HANNA, L., ZICHOSCH, J., JAWETZ, E., VAUGHAN, D. G., Jr. & THYGESON, P. **Virus isolated from Inclusion Conjunctivitis of Newborn (Inclusion Blennorrhea).** *Science.* 1960, Dec. 2, v. 132, 1660–61, 1 fig.

This paper reports the isolation of a virus, with the morphological characters of the psittacosis-LGV group, from a case of inclusion blennorrhoea diagnosed clinically and by microscopy. 7-day embryonated eggs were inoculated by the yolk-sac route with a suspension of conjunctival scrapings and incubated at 35°C. Blind passage was made at 7-day intervals [*Trop. Dis. Bull.*, 1960, v. 57, 1114]; at the 5th some eggs died and virus was seen in yolk-sac smears; it was well established to growth in the egg by the 9th passage. No success was obtained in 9 other clinically similar cases. 2 cynomolgus monkeys and 1 baboon developed a mucopurulent conjunctivitis 5 days after receiving this virus by conjunctival instillation. In neither the human host nor the infected apes did this virus affect the cornea.

S. P. Bedson

POLLARD, M., STARR, T. J., TANAMI, Y. & ELLIOTT, A. Y. **Cytochemical Effects of Substituted Pyrimidines on Psittacosis Virus.** *Proc. Soc. Exper. Biol & Med.* 1960, Dec., v. 105, No. 3, 476–8, 4 figs. [14 refs.]

Making use of acridine orange staining and fluorescence microscopy the authors followed the development of psittacosis virus in cultures of human synovial cells. In the course of the first 14 hours of cultivation RNA-staining material developed around the DNA-staining infective virus particles forming red-orange cytoplasmic inclusions: this is called the "red-ball" stage. RNAase treatment of these inclusions at 14 hours dissipated the RNA matrix revealing immature virus particles, which were Feulgen-positive, non-infective for mice intracerebrally and unattractive to fluorescein-tagged antibody. Subsequently, in the next 48 hours or so, the RNA-staining material changed in colour from red to orange to yellow and finally to green and eventually the inclusions were seen to consist of mature virus particles which were DNA-staining, antigenic and infective. 5-fluorouracil or 5-fluoro-orotic acid when added to the cultures at the "red-ball" stage stopped virus multiplication. It is suggested that these substances—substituted pyrimidines—act by interfering with protein synthesis.

S. P. Bedson

JAWETZ, E. & HANNA, L. **Trachoma Viruses isolated in the United States. 2. Assay of Egg Infectivity and Stability.** *Proc. Soc. Exper. Biol & Med.* 1960, Nov., v. 105, No. 2, 207–10, 1 fig. [14 refs.] **3. Strain Specific Effects of Tetracycline and Penicillin.** *Ibid.*, 320–23, 2 figs. [11 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 637.]

TRLIFAJOVÁ, Jarmila. Kultivace viru vakcinie na tkánových kulturách z celých myších embryí. **[Cultivation of Vaccinia Virus on Tissue Cultures from Whole Embryos of Mice]** *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1961, v. 10, No. 1, 7–10, 3 figs. on 2 pls. [27 refs.]

The English summary appended to the paper is as follows:—

"It has been found that it is possible to cultivate the vaccinia virus on tissue cultures from mice embryos; by such a cultivation, the characteristic cytopathogenic effect is caused. The specificity of the caused changes was proved by neutralizing the virus with the immune serum and by a control inoculation on chorioallantois."

SZÁNTÓ, J. Izolácia bunkových kmenov z pľúcneho tkaniva králika a krysy. II. Rozmnožovanie a cytopatogénny efekt vírusu herpes simplex. **[Isolation of Cell Strains from Lung Tissue of Rabbit and Rat. II. Multiplication and Cytopathogenic Effect of the Virus of Herpes Simplex]** *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1961, v. 10, No. 1, 11–17, 10 figs. on 3 pls. & 1 graph. [13 refs.]

The English summary appended to the paper is as follows:—

"The virus of herpes simplex multiplies intensively in cells of stable strains ZP-1/58 and KrP-2/58 having been isolated from lung tissue of rabbit and rat. The

virus multiplies in these cells to the same degree in the presence of a cultivation medium with 5–10 p.c. of inactivated or native serum, or only in the presence of the synthetic medium 199 or of the Hank's solution. The cells ZP-1/58 and KrP-2/58 are apt for the titration of the herpes simplex virus, too.

"The strain of the herpes simplex virus having been passaged on chorioallantoic membrane of chicken embryos, which was used in the experiments, caused cytopathogenic changes of a non-proliferative type in tissue cultures of chicken embryo cells. After passages of the same virus of herpes simplex on cells of ZP-1/58 and KrP-2/58, changes of a giant cell-like character were caused in these cells. Cytopathogenic changes of that type were caused by the so passaged virus thereafter even in cultures of chicken embryonic cells."

ARTZET, F. Antigène herpétique fixant le complément. [**Studies on Complement-Fixing Herpetic Antigen**] *Ann. Inst. Pasteur.* 1960, Nov., v. 99, No. 5, 777–83. [19 refs.]

24–36 hours after infection, rabbit kidney cells contained herpes simplex complement-fixing antigen while none could be detected in the culture medium. 48 hours after infection, antigen was present in the medium but could no longer be detected within the cells. The most concentrated preparations of complement-fixing antigen were prepared by recovering cells 24 hours after infection, suspending them in a small volume of buffer and then disrupting them by freezing and thawing.

Janice Taverne

PARNAS, J., SZCZYGIELSKA, J., ZWOLSKI, W. & BURDZY, K. Wrażliwośc *Microtus arvalis* i niektórych stawonogów na zakażenie wirusem grypy. [**Susceptibility of *Microtus arvalis* and some Arthropoda to Infection with the Virus of Influenza**] *Wiadomości Parazytologiczne.* Wrocław. 1960, v. 6, No. 6, 529–31.

The English summary appended to the paper is as follows:—

"The experiments I and II were conducted on 2 white mice, 5 *Microtus arvalis*, 2 *Gamasides*, 91 *Hoplopleura acanthopus* and 200 *Polyplax spinulosa*.

"For the experiments the influenza virus PR8 was used.

"As regards *Microtus arvalis* it was proved that it is susceptible to the virus of influenza PR8. The susceptibility of *Microtus arvalis* proved to be not lower than that of white mice. The virus of influenza PR8 was isolated from the lungs of all the examined white mice and *Microtus arvalis*. In not a single case, however, could the virus be isolated from the *Gamasides*, neither from the *Hoplopleura acanthopus* nor from the *Polyplax spinulosa* in spite of the fact that undoubtedly in all the examined mice the virus infection ran in the form of viraemia.

"This is an indication that the *Gamasides*, *Hoplopleura acanthopus* and *Polyplax spinulosa* could not be infected with the virus of influenza PR8 (or that the virus was destroyed after the penetration to the organism of the *Arthropoda* with the blood of the host).

"The experiments should be repeated on a larger material and the viraemia of mice should be submitted to control. It appears that *Microtus arvalis* is a suitable animal for experimental infection with the virus of influenza."

HAUSLER, W. J., Jr. & DICK, E. C. **The Purification and Concentration of Influenza A Virus (PR8) by a Method of Continuous Extraction with Glycine of a Zinc-Virus Precipitate.** *J. Infect. Dis.* 1960, Sept.–Oct., v. 107, No. 2, 189–94, 1 fig. [21 refs.]

This paper presents a modification of the technique described by METCALF [this *Bulletin*, 1957, v. 32, 1201] since continuous extraction with glycine was used instead of repeated extractions. Crude infected allantoic fluid (CAF) was chilled to 2°C. and 0·1 M zinc acetate added to give a final concentration of 5 ml. per litre of CAF. After 10 minutes the zinc-protein complex was sedimented at 2,600 g for 12 minutes at 2°C. and extracted with 1·0 M glycine and the zinc then removed on an exchange resin column containing Amberlite IR–120 (Na). [The apparatus is described.] The resin effluent was then subjected to one high speed centrifugation followed by one low speed and a final high speed centrifugation. The resulting pellet was resuspended in phosphate buffer and diluted to one-twentieth of the volume of the original CAF.

Volumes ranging from 660 ml. to 1350 ml. were handled. A 20-fold reduction in volume was accompanied by a 20-fold rise in haemagglutination (HA) titre and a 5- to 10-fold decrease in protein nitrogen. In different experiments one product contained 444,000 HA units per mgm. protein and another 1,580,000 HA units per mgm. protein nitrogen. One of the preparations tested had a low infectivity in embryonated eggs and electron micrographs showed particles of 102·6 to 111·9 mμ mean diameter. The micrographs also revealed that a considerable quantity of extraneous material had been removed; this was supported by ultraviolet adsorption spectroscopy. The purified antigen produced haemagglutination-inhibition titres 1-fold lower than the crude fluid with 18 of 25 sera tested. *D. Taylor-Robinson*

POLYAK, R. J. & SMORODINTSEV, A. A. **Electrophoretic Investigations on Thermostable Inhibitors of Type A2 Influenza Virus in Normal Animal Sera.** *Acta Virologica.* Prague. 1961, Jan., v. 5, No. 1, 1–3, 3 figs. on 3 pls.

The inhibitory activity of normal horse, guineapig and rabbit sera for 3 1957 A2 virus strains increased 4 to 6-fold after heating the sera at 60°C. for 1 hour. This suggested that the inhibitor was possibly not of protein nature. However, paper electrophoresis was carried out on 8 horse and 10 guineapig sera; some paper strips were fixed and stained for proteins and others cut into sections and each of the sections eluted with saline and the eluate tested for inhibitory activity in the

haemagglutination-inhibition test. The activity of both unheated and heated sera was confined to the protein fractions (12 to 16) corresponding to a mobility higher than alpha 2 globulins. On the other hand, the thermolabile beta lipoprotein inhibitor for A1 viruses was confined to fraction 9 and had a mobility similar to that of gamma globulin. *D. Taylor-Robinson*

KRIZANOVÁ-LAUCÍKOVÁ, O., SZÁNTÓ, J. & KOCISKOVÁ, D. **Purification and some Properties of the Thermostable Inhibitor against Avid A2 Influenza Virus from Horse Serum.** *Acta Virologica.* Prague. 1961, Jan., v. 5, No. 1, 4–11, 3 figs. (1 on pl.). [24 refs.]

It has been shown by many workers that sera may contain heat stable inhibitors of haemagglutination by influenza A2 viruses, which are distinct from the Francis or alpha inhibitors active against other influenza viruses. Horse serum was precipitated with sulphosalicylic acid and the filtrate was lyophilized and extracted with phenol-water mixtures at 65°C. The purified glycoprotein fraction thus obtained in the water phase was electrophoretically homogeneous and showed 6,554–13,107 units of inhibitory activity and 512–1,024 units of virus neutralizing activity per mgm. The inhibitory activity was destroyed by prolonged treatment with trypsin and was unaffected by 2 hours treatment with RDE, which released about 50% of the sialic acid.

D. A. J. Tyrrell

KRIZANOVÁ-LAUCÍKOVÁ, O., SZÁNTÓ, J. & KOCISKOVÁ, D., RUTTKAY-NEDECKÝ, G. & SOKOL, F. **Differences in the Properties of Two Inhibitors against Avid A2 Influenza Virus Strains from Horse Serum.** *Acta Virologica.* Prague. 1961, Jan., v. 5, No. 1, 12–18, 5 figs. (2 on pl.).

Following their other experiments [see above] the authors treated horse serum with butylnaphthalene sulphonate (Neokal) and found "the bulk of" the inhibitory activity of what they call the "gamma-globulin inhibitor" in the precipitate thus formed. This material contained 409–1638 units of haemagglutination inhibiting activity and 512–1024 units of virus neutralizing activity per mgm. On electrophoresis it contained mainly a slow-moving component and on ultracentrifugation it contained components of sedimentation constants 5·9 S and 14·7 S. Neokal did not precipitate the glycoprotein inhibitor and sulphosalicylic acid precipitated the "gamma-globulin inhibitor", and the activity of the latter was heat labile. They could therefore be distinguished from each other. The "gamma-globulin inhibitor" reacted with different viruses from those reacting with beta-inhibitor of bovine serum and did not combine with non-avid influenza A2 viruses as does antibody.

[It seems possible to the abstracter that in spite of careful separations the inhibitory activity of the fractions described is due not to the main chemical component but to a small amount of a very active substance. Zone electrophoresis separated the alpha inhibitor activity from the main electrophoretic component of purified human serum glycoprotein (TYRRELL, this *Bulletin,* 1955, v. 30, 183).]

[See also below.] *D. A. J. Tyrrell*

KOCISKOVÁ, D., STYK, B. & HÁNA, L. **The Relation of Properdin and Complement to the Thermolabile Cofactor of Normal Serum necessary for the Reaction of Specific Antibody with Influenza A2 Virus.** *Acta Virologica.* Prague. 1961, Jan., v. 5, No. 1, 19–25.

Continuing their experiments [this *Bulletin,* 1960, v. 35, 89; see below] the authors tested the relation between "cofactor" and properdin by removing properdin from mouse serum by treatment with zymosan; treated sera functioned as co-factor. Also purified properdin had no activity as co-factor. Human serum functioned as co-factor after it had been freed of complement by treating it with antigen-antibody complexes and with zymosan; the co-factor activity dropped 4-fold while the titres of each component of complement dropped several hundred-fold. Some experiments with sera freed of single components of complement were difficult to interpret since those freed of component 1 and 4 (R1 and R4) had no co-factor activity. The authors concluded however, that "the cofactor is not identical with properdin" and neither is "whole complement nor its components". *D. A. J. Tyrrell*

HÁNA, L., STYK, B. & KOCISKOVÁ, D. **Estimation of the Distribution and the Character of Inhibitors against "Avid" A2 Influenza Virus Strains in Protein Fractions of Guinea Pig and Horse Sera obtained by Paper Electrophoresis.** *Acta Virologica.* Prague. 1960, Nov., v. 4, No. 6, 356–64, 8 figs. on 8 pls. [24 refs.]

Sera of guineapigs and horses contain a non-specific inhibitor for "avid" influenza A2 viruses. The authors separated these sera by electrophoresis on filter paper at *p*H 9. Parallel strips were stained for protein, glycoprotein or lipid, and eluted into saline for assay of haemagglutination inhibiting (HI) or virus neutralizing (VN) activity. Slightly different methods were used in performing electrophoresis for subsequent examination by different methods. HI and VN activity was found mainly in the alpha 2 globulin region, where glycoprotein staining was maximal. There was one type of horse serum in which inhibiting activity was distributed throughout the globulins. On electrophoresis at low *p*H (4·2) inhibiting activity and glycoprotein moved with—or in front of—albumin and was resolved into several components. The authors are "of the opinion however that in unheated sera the HI activity is bound to glycoproteins". *D. A. J. Tyrrell*

STYK, B. & HÁNA, L. **Investigations into Specific Antibodies against A2 Influenza Viruses and the Thermolabile Co-factor by means of Paper Electrophoresis.** *Acta Virologica.* Prague. 1960, Nov., v. 4, No. 6, 365–70, 3 figs. on 3 pls. [10 refs.]

It has been shown [STYK, *et al.*, this *Bulletin.* 1959, v. 34, 501] that when mice are immunized against influenza

A2 virus and serum antibody titrations are made with non-avid strains of virus then the first antibodies produced appear to be heat-labile because they can only inhibit haemagglutination in the presence of a heat-labile co-factor present in normal sera. Further studies of this experimental system are reported here. Serum was separated by electrophoresis on paper and the eluates were titrated by haemagglutination inhibition in the presence of heated immune serum to demonstrate the presence of co-factor, and in the presence of unheated non-immune serum, to demonstrate antibody. It was found that antibody activity was associated with the fast-moving gamma globulins while co-factor activity was associated mainly with beta globulins.

D. A. J. Tyrrell

HAMBURG, V. P. **Study of the Properties of a Serum Inhibitor of Type A2 Influenza Virus.** *Problems of Virology.* London. 1960, v. 5, No. 3, 365–70. [17 refs.] [Translated from Russian.]

"(1) In horse sera an inhibitor of the haemagglutinins of the Singapore strain of type A2 influenza virus was found in high titres. Virus-neutralizing activity was not by any means displayed by all the fresh sera but it appeared in many of them on storage at 4°.

"(2) In the organs and tissues of the rabbit, inhibitor of virus haemagglutination was either not found or was present in low titres.

"(3) By means of anti-inhibitor antisera prepared by immunizing chicks and mice the antigenic identity of the inhibitor of virus haemagglutination of human and horse sera was established. The anti-inhibitor antiserum did not neutralize the virus neutralizing factor of normal human and horse sera in chick embryo experiments."

KORNYUSHENKO, N. P. & MAXIMOVICH, N. A. **Intrauterine Transmission of Influenza Infection in Experimental Animals.** *Acta Virologica.* Prague. 1961, Jan., v. 5, No. 1, 26–30, 4 figs. on 2 pls.

This study was stimulated by the isolation of influenza A2 virus from the lungs of several infants who died with pneumonia within 2 days of birth.

Pregnant mice, rats, guineapigs and rabbits were inoculated intranasally with 0·02 ml., 0·05 ml., 0·5 ml. and 0·5 ml., respectively, of mouse-adapted influenza A (PR8) virus (10^8 LD50/0·05 ml.). 10 pregnant mice inoculated 3–4 days before delivery died with pneumonia within 2–6 days. Virus was isolated, in chick embryos, from the amniotic fluid and foetal membranes in 6 of these pregnant mice. Virus was detected by direct haemagglutination as well as by chick embryo isolation in 19 of 29 embryos and newborn mice; 24 of these were also examined histologically. Despite the presence of virus there were no distinctive pulmonary changes in mice examined just before or just after birth. However, in 5 newborn mice examined up to the 5th day after delivery there were changes characteristic of influenza virus infection. Virus was also isolated from the lungs and foetal membranes of 5 of 7 rats and from the lungs of 4 of 26 newborn rats but in none of the latter were there histological changes. Although virus could not be isolated from newborn guineapigs and rabbits, virus was recovered from foetal membranes—further evidence of transplacental passage.

[The precautions taken to prevent accidental infection of membranes and embryos are not described but with the mice, at least, the amount of virus present to cause direct haemagglutination must have been more than could be accounted for by accidental contamination.]

D. Taylor-Robinson

POLIAK, R. I. **Virus-Neutralizing Activity of β-Lipoprotein Fraction of Normal Sera of Various Animals.** *Problems of Virology.* London. 1960, v. 5, No. 1, 68–74, 2 figs. [12 refs.] [Translated from Russian.]

The sera of normal rabbits, guineapigs, mice and rats were fractionated by BORNSTEIN'S modification of COHN'S method (*Biochim. et Biophys. Acta,* 1956, v. 20, 522). The β-lipoproteins of fraction III were obtained and were able to neutralize the infectivity of a strain of influenza virus except in the case of rat sera, when the original serum had little neutralizing activity. The neutralizing activity of the β-lipoprotein was preserved for 2 weeks at 4°C. but destroyed by heat at 62° for 1 hour and was not extracted with the lipids by Tween 80. The author points out that although some have thought that these serum non-specific inhibitors were identical with properdin [this *Bulletin,* 1957, v. 32, 517] his results are further evidence that the two substances are biochemically different, for properdin is euglobulin precipitated as fraction I by Cohn's method and its biological activity is unstable.

[From table 2 it appears that the original serum often neutralized over 10 times more virus than the serum fractions. However, table 1 shows that a 4-fold dilution in serum or protein fraction produce a 100-fold drop in the amount of virus neutralized. It is therefore probable that most of the neutralizing activity of the original serum was recovered in the β lipoprotein fraction but this point is not really brought out in the paper.]

D. A. J. Tyrrell

BERTI, T., VISENTINI, P. & MENEGHELLI, P. Ricerche di chemioterapia antivirale. II. Azione del composto P8 sull'influenza sperimentale nell'embrione di pollo e nel topo. [**Studies on Antiviral Chemotherapy. II. Action of Compound P8 on Experimental Influenza in Chick Embryos and Mice**] *Giorn. di Microbiol.* Naples. 1960, July–Sept., v. 8, No. 3, 159–68, 1 fig. [11 refs.]

The English summary appended to the paper is as follows:—

"The compound P 8, a complex of bismuth and pyrocatechin sodium disulfonate, noticeably inhibits the growth of NDV and influenza virus in the chick embryo, also if injected in the allantoic cavity 10 hours after the virus. However it has not virucidal activity *in vitro.*

"In mice infected with influenza A PR 8 there was observed some protective activity on the three considered

effects (lethality, pulmonary index, number of viruses in the lungs).

"On the ground of the obtained results there is discussed the mode of antiviral action of the compound P 8 and there is proposed an interpretation of the discrepancy between the noticeable activity in the chick embryo and the relatively slight activity against experimental influenza in mice."

HOLPER, J. C., MILLER, L. F., CRAWFORD, Y., SYLVESTER, J. C. & MARQUIS, G. S., Jr. **Further Studies on Multiplication, Serology and Antigenicity of 2060 and JH Viruses.** *J. Infect. Dis.* 1960, Nov.–Dec., v. 107, No. 3, 395–401, 3 figs.

The authors grew JH and 2060 viruses in primary monkey kidney cultures containing "islands" of cells (about 4 days after seeding). Stationary cultures at 36° C. produced $10^{1.5}$ to 10^4 TCID50 (Tissue Culture Infectious Doses). Rolled cultures, however, yielded 10^5 and 10^6 TCID50 per 1·0 ml. fluid with inocula of 10^2 and 10^4 TCID50, respectively. 2 to 3 injections of material of 10^5–10^6 TCID50 were given to guineapigs [amount and site of injection not stated] over a period of 2 to 3 weeks; the neutralization titres of the sera thus obtained ranged from 1 in 8 to 1 in 256. Inoculation of either agent produced sera which were able to neutralize both viruses to approximately the same titre. 2 ferrets and 2 rabbits did not produce antibody after the same course of injections. Virus pools (10^5–10^6 TCID50) were inactivated with formaldehyde [time and concentration not stated] and injected into volunteers who were in 3 groups of 10. 2 injections were given [route and timing not stated]. Antibody rises occurred in the sera of most volunteers against both viruses irrespective of which virus was used in the vaccine.

100 paired sera were collected from recruits at the Great Lakes Naval Training Station during the winter of 1958–59. There was a 4-fold or greater increase in neutralizing antibody titre against JH or 2060 virus in 14 of 37 sera from febrile respiratory cases, 6 of 33 from afebrile respiratory cases and 13 of 30 sera from patients without respiratory disease. Since, in particular, there is no report of the isolation of JH or 2060 viruses, "the relationship of these viruses to disease is not clear from this study". *D. Taylor-Robinson*

EPSTEIN, M. A. & POWELL, A. K. **The Isolation of Type 5 Adenovirus using a Fluorocarbon; combined Morphological and Biological Studies.** *Brit. J. Exper. Path.* 1960, Dec., v. 41, No. 6, 559–66, 7 figs. on 4 pls. [23 refs.]

In the study of adenovirus type 5 by electron microscopical and cytochemical means, certain preliminary experiments were carried out. Infected HeLa cell cultures were incubated at 37°C. for 3 days. The cells were then detached by shaking and centrifuged at low speed. The cell pellets so formed were treated with 3 applications of Arcton 113 and the final aqueous layer was ultracentrifuged; the resulting pellets were fixed with permanganate, dehydrated, and embedded and then serial sections cut from various levels were examined with an electron microscope.

The pellets contained a dense white zone which consisted almost entirely of uniform particles measuring about 60 mμ in diameter. The particles were scattered randomly, although occasionally aggregated in arrays of possible crystalline structure, and were hexagonal with a central electron-dense nucleoid. On titration in HeLa cells the dense white zone was found to be the most infectious part of the pellet; it was concluded that the particles contained within this zone were of virus nature. A very thin basal layer to the dense white zone contained cell debris; this consisted of round, relatively large elements and membrane-bounded structures. A firm jelly, which covered and merged into the other regions, was made up of fine beaded threads. *D. Taylor-Robinson*

EPSTEIN, M. A., HOLT, S. J. & POWELL, A. K. **The Fine Structure and Composition of Type 5 Adenovirus; an Integrated Electron Microscopical and Cytochemical Study.** *Brit. J. Exper. Path.* 1960, Dec., v. 41, No. 6, 567–76, 11 figs. (4 coloured) on 4 pls. [28 refs.]

Pellets of purified virus were prepared by ultracentrifugation of fluorocarbon-treated suspensions [see EPSTEIN and POWELL above]. Samples from the dense white zone were examined by electron microscopy. Hexagonal adenovirus particles contained nucleoids; the latter were 35 mμ in diameter and were surrounded by a viroplasm 12 mμ wide. Further, the nucleoids contained threadlike elements arranged in a parallel curving array. Virus preparations were fixed with permanganate and treated with buffer at *p*H 9 and then with deoxyribonuclease (DNase) which removed the nucleoids. Further evidence that deoxyribonucleic acid was localized in the nucleoid was provided by fluorescence microscopy; smears of the dense white zone, treated with buffer at *p*H 9 and stained with acridine orange, showed a green fluorescence in ultra-violet light which was abolished after digestion with DNase.

D. Taylor-Robinson

MONACI, V., VITALI-MAZZA, L., TARDINI, A. & VERDI, G. P. Ricerche al microscopio elettronico sulla morfologia e sullo sviluppo dell'adenovirus tipo 8 in cellule KB. **[Studies with the Electron Microscope on the Morphology and Development of Adenovirus Type 8 in KB Cells]** *Ann. Sclavo.* Siena. 1960, Nov.–Dec., v. 2, No. 6, 631–44, 16 figs. on 13 pls. [30 refs.] English summary (7 lines).

CHANOCK, R. M., FOX, H. H., JAMES, W. D., BLOOM, H. H. & MUFSON, M. A. **Growth of Laboratory and Naturally Occurring Strains of Eaton Agent in Monkey Kidney Tissue Culture.** *Proc. Soc. Exper. Biol. & Med.* 1960, Nov., v. 105, No. 2, 371–5. [15 refs.]

Roller tube cultures of rhesus kidney cells, chick kidney cells and Hep II cells were prepared and maintained in a medium containing 5% chick serum, Eagle

medium containing double the usual concentration of vitamins and amino acids, and 2,000 units per ml. of penicillin, the only antibiotic. The inoculum consisted of a pool of the FH strain of Eaton agent, propagated in embryonated eggs or of throat swabs from patients with pneumonia. The presence of the agent and its concentration were determined by inoculating serial dilutions of culture fluid or disrupted cells into embryonated eggs, incubating these eggs for 6 days at 35°C. and then examining frozen sections of the embryo lung by the fluorescent antibody method for the presence of the antigen of the Eaton agent. In this way it was shown that the agent probably multiplied in the cultures used; however it was not possible to detect specific antigen in the tissue culture cells. The maximum titres ($10^{4\cdot2}$ egg infectious doses/ml.) were obtained in cultures of monkey kidney cells, and 3 serial passages were successfully performed. 17 throat swabs were inoculated into monkey kidney cultures. The fluids of the cultures were collected at 7, 10 and 15 days of inoculation, inoculated into eggs and tested with fluorescent antibody. By this technique the agent was recovered from 14 throat swabs. 3 of the strains seemed to be antigenically similar to the laboratory strain. *D. A. J. Tyrrell*

Gordon, F. B., Quan, Alice L., Cook, M. Katherine, Chanock, R. M. & Fox, H. H. **Growth of the Eaton Agent of Primary Atypical Pneumonia in Chick Entodermal Tissue Culture.** *Proc. Soc. Exper. Biol. & Med.* 1960, Nov., v. 105, No. 2, 375–7.

Entodermal cell cultures were prepared from 4-day chick embryos and grown on circular coverslips in flat bottom tubes to which 0·5 ml. of a mixture of 25% of chicken serum and 75% of Hanks saline were added. Cultures were incubated at 36–37°C. Two culture series were initiated with a suspension of agent purified from a suspension of chick embryo lung and trachea. The fluids of the cultures were passed at the 5th or, better 11th day in the first series and on the 7–9th day in the second series. There was no cytopathic effect but the agent was detected by chick embryo inoculation of the 10th passage fluid of the first series and the 6th passage fluid of the second. The agent could not be demonstrated in the tissue culture cells by staining with fluorescent antibody. The authors conclude that they have propagated the agent in tissue culture.
D. A. J. Tyrrell

Gudnadóttir, Margrét G. **Studies of the Fate of Type 1 Polioviruses in Flies.** *J. Exper. Med.* 1961, Jan. 1, v. 113, No. 1, 159–76, 8 figs. [15 refs.]

The survival of type 1 poliovirus (mainly LSc strain but a few experiments were done with Mahoney) fed to flies was investigated by using a plaque system of virus assay. One experiment was done with *Musca domestica* and the rest with *Phormia regina*. It was found that virus survived at least 4 days and often as long as 11 days after feeding. The virus titre in faeces or carcass was proportional to the amount of virus fed. After an initial decline, virus titres in the carcass and faeces both rose in parallel to a new peak, and sometimes to a second peak. The results strongly suggest that virus multiplication occurs, probably in the gut of the flies. These flies were probably important means of spread of poliovirus in nature. It was also found that virus survived for 3 months in hibernating flies, suggesting that poliovirus could overwinter in them. *A. J. Beale*

Pintus, L. Modificazioni morfologiche delle cellule KB infettate con virus poliomielitico tipo 1. **[Morphological Changes in KB Cells Infected with Type I Poliomyelitis Virus]** *Giorn. di Batteriol., Virol. ed Immunol.* 1960, July–Oct., v. 53, Nos. 7/10, 332–41, 13 figs. English summary.

Pitzurra, M., Guaitini, V. & D'Angelo, L. Studio dell'effetto citopatogeno di virus polio tipo 1 su vetrini fissati e colorati. **[Study of the Cytopathogenic Effect of Type 1 Poliovirus on Fixed and Stained Slides]** *Ann. Sclavo.* Siena. 1960, Nov.–Dec., v. 2, No. 6, 569–76, 6 coloured figs. on pl. English summary (7 lines).

Norrby, E. C. J. & Albertsson, P. Å. **Concentration of Poliovirus by an Aqueous Polymer Two-Phase System.** [Correspondence.] *Nature.* 1960, Dec. 17, v. 188, 1047–8. [10 refs.]

A practical method for concentrating and purifying poliovirus that should be applicable to the problems of manufacturing potent killed poliovaccine is described. The method used is essentially as described by Philipson *et al.* [this *Bulletin*, 1960, v. 35, 1245]. Poliovirus as infected monkey kidney was clarified by centrifugation. Thereafter 0·2% dextran sulphate and 6·45% polyethylene glycol (6000 Mol. Wt) were added together with sufficient 5 M sodium chloride to make the final salinity 0·3 M. After careful mixing the system was allowed to settle out at 4°C. The solutions separate and the virus accumulates almost completely in the dextran sulphate phase nearly 100 times concentrated. The virus was in 17% dextran and rather viscous and inconvenient for vaccine preparation. The virus can be removed from the dextran by the addition of 5 M sodium chloride till the molarity of sodium chloride reaches 1 M. The system then settles out again but this time the virus is in the top phase, which is again of smaller volume, and the dextran in the bottom phase. The virus fluid is now approximately 100- to 500-fold concentrated and is also purified. The residual 0·1% dextran (the virus also contains approximately 1% polyethylene glycol) can be removed by precipitation either with 3 M potassium chloride or 1 M barium chloride. All the virus remains in solution. *A. J. Beale*

NOMURA, S.; TAKEMORI, N. **Mutation of Poliviruses with respect to Size of Plaque. I. Selection of Minute Plaque Mutants of Three Types of Polioviruses in Tissue Cultures** [NOMURA & TAKEMORI]. *Virology*. New York. 1960, Oct., v. 12, No. 2, 154–70, 8 figs. [18 refs.] **II. Reverse Mutation of Minute Plaque Mutant** [TAKEMORI & NOMURA]. *Ibid.*, 171–84, 4 figs. [28 refs.]

I. The authors describe the selection of certain m mutants of the 3 types of poliovirus which are characterized by the production of very small (minute) plaques on susceptible cells [this *Bulletin*, 1958, v. 33, 409]. Observation and enumeration of these plaques is exceedingly difficult owing to their small size and it is also thought that many m mutants do not produce any visible plaques at all. The presence of these mutants is therefore assessed by comparing the plaque count (large plaques) with the TCD50 determined by observing cytopathic effects in test tube cultures in a fluid medium. These m mutants of the MEF–1 strain of type 2 virus were readily obtained by serial passage in HeLa cells. They were more rapidly selected in the presence of 20–40% normal bovine serum than in 2% calf serum or in 1% horse serum. Type 2 mutants could also be selected by serial culture in the FL strain of human amnion cells. Similarly, m mutants of the Saukett strain of type 3 poliomyelitis virus were obtained by serial passage in HeLa cells in 20% normal bovine serum. They were also obtained by serial passage in a clone of FL cells (FL 19) which is resistant to cellular destruction by infection with the m^+ Saukett virus while still retaining susceptibility to destruction by type 1 and 2 poliomyelitis virus. Attempts to select m mutants from type 1 Mahoney poliovirus were unsuccessful until a strain of FL cells was obtained which was resistant to destruction by the Mahoney strain. This line of FL cells was obtained as a result of curing a persistent infection with type 2 virus with antiserum. The serial passage of Mahoney virus in these cells in 20% normal bovine serum yielded m mutants. The m mutants did not differ antigenically from the m^+ parental viruses nor did they differ in their rate of growth nor in their destructive effect on cells in the absence of an agar overlay. It is thought that the small size is caused by some component of the agar overlay system.

II. The rate of back mutation of m strains to m^+ was studied. Small numbers of m^+ mutants could easily be detected by plaque counts. It was found that several m mutant stocks contained between 10^{-4} and $5{\cdot}5 \times 10^{-5}$ proportion of m^+ reverse mutants. The rate of mutation was found to be 3×10^{-7} for m–543 mutant of MEF–1.

It was found that a substance extracted from agar overlay medium (1·5% Difco or Japanese agar and lactalbumin yeast extract medium) inhibited the growth of m mutants. This was not an *in vitro* effect of the virus but an effect on the growth in cells (HeLa, FL amnion or monkey kidney). The inhibitory effect of agar overlay extract on the growth of m mutants provided an excellent selective medium for the detection of small numbers of m^+ back mutants. *A. J. Beale*

ARTZET, Françoise, with the collaboration of M. L. RYHINER. Antigène poliomyélitique pour fixation du complément. [**Preparation of a Poliomyelitis Antigen with a view to Complement Fixation**] *Ann. Inst. Pasteur*. 1960, Dec., v. 99, No. 6, 852–8.

The preparation of complement-fixing antigens from all 3 types of poliovirus is described. The highest titre antigen of all 3 types grown in KB cells was obtained as follows: cells were infected at a multiplicity of 4–5 and after 24 hours the cells were harvested and sedimented from the culture medium. The cells were then resuspended in 1 in 20 volume of veronal buffer and frozen and thawed 5 times. This antigen gave higher antigen titres (and detected higher antibody titres) than the supernatant culture fluid or cell extract after 48 hours incubation. No complement fixation occurred with normal cell extracts and no difficulty was experienced with anticomplementary antigens. *A. J. Beale*

MCINTOSH, B. M. **Susceptibility of Some African Wild Rodents to Infection with Various Arthropod-Borne Viruses.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1961, Jan., v. 55, No. 1, 63–8. [28 refs.]

About 500 LD50 of virus was inoculated intraperitoneally or intracardially into groups of wild caught rodents which were bled in rotation and viraemia tested for by inoculation of mice. Neutralizing antibody was tested for before inoculation and about 3 weeks later.

Wesselsbron, Spondweni and Pongola viruses failed to circulate in *Mystromys, Mastomys, Saccostomus, Aethomys* and *Tatera*. Pongola and Spondweni also failed to circulate in *Lemniscomys* and Wesselsbron in *Otomys*. None developed neutralizing antibody to these three viruses. West Nile virus neither circulated nor caused antibody formation in *Mystromys, Arvicanthis, Mastomys, Otomys* and *Rhabdomys*. In *Aethomys* 1·5 log of virus circulated on the 1st and 2nd day after inoculation and 1 of 2 developed antibody. Bunyamwera virus circulated at a titre of 1 log on the 1st and 2nd day in *Mystromys* and 4 of 5 developed antibody: 2 of 5 *Arvicanthis* but not *Mastomys* developed antibody and neither circulated virus. Chikungunya virus circulated at titres of 2·5–6·4 log for the first 5 days in *Mystromys* maximal on the 3rd day. It also circulated at 1·5–2·5 log on the 2nd or 3rd day in *Arvicanthis, Mastomys* and *Aethomys* but not in *Saccostomus* or *Tatera*. All of these species developed antibody except only 1 of 4 *Saccostomus*.

Middelburg virus circulated in all the species tested except *Mastomys*: titres over 3·5 log were reached in *Mystromys, Aethomys, Saccostomus* and *Tatera* the longest duration being 4 days in *Saccostomus* although *Tatera* circulated virus on days 1, 2 and 5 Most of the animals tested developed antibody. H336 virus [related to Uganda S] circulated for at least 4 days reaching 3·5 log or more in all species tested except *Mastomys* in which it circulated only on days 1 and 2. All species tested developed antibody except *Mastomys*. Simbu virus circulated for 4 days in *Mystromys* (2·1, 2·5 log),

and from the 2nd to the 5th day (1·5–4·1 log) in *Saccostomus*. Little or no circulation of virus occurred in *Arvicanthis*, *Mastomys* or *Tatera*. Only 1 of 3 *Mastomys* and *Arvicanthis* and 1 of 4 *Tatera* developed antibody.

Rift valley fever virus circulated until about the 4th day in *Mystromys* (trace to 3·3 log), *Mastomys* (trace to 1·5 log) *Aethomys* (1·4–4·2 log) and *Saccostomus* (trace to 6 log) but not in *Tatera*. Only 4 of 4 *Mystromys* and 1 of 5 *Mastomys* developed antibody. Germiston virus was tested only in *Tatera* in which it circulated for 7 days with maximum titres over 6 log and 2 of 3 developed antibody. The general low incidence of antibody response (64% of animals which had had viraemia) may have been due to dilution of the sera (1:5). None of the animals showed illness except *Saccostomus* with Rift Valley fever. *C. E. Gordon Smith*

HALE, J. H. & PILLAI, K. **Observations on the Haemagglutinating Activity of the Arthropod-Borne Viruses.** *Ann. Trop. Med. & Parasit.* 1960, June, v. 54, No. 2, 236–46.

Haemagglutinins were prepared from group B arthropod-borne viruses by standard methods. Filtration and centrifugation did not separate infectivity from haemagglutinin. Storage of haemagglutinin and infectivity at *p*H 6·0–11·0 was studied: at acid *p*H haemagglutinin was rapidly destroyed but infectivity more slowly; at alkaline *p*H haemagglutinin was very stable but infectivity was slowly lost. A Japanese encephalitis haemagglutinin was mixed with chick erythrocytes at *p*H 6·5–9·0 and after 2 hours centrifuged. Haemagglutinin was completely removed only at *p*H 6·5 and partially at *p*H 6·8. The sedimented cells were washed then suspended at *p*H 5·0–7·6: haemagglutination occurred at *p*H 5·0–7·0 with mixtures originally at *p*H 6·5, 6·8, 7·0. Erythrocytes could not be sensitized in this way by dilute haemagglutinins reacting with concentrated cell suspensions and with concentrated haemagglutinins and weak cell suspensions lysis occurred. Erythrocytes from chicks up to 18 days old were satisfactory but not those from adult fowls. When cells sensitized at *p*H 6·8 with Japanese encephalitis haemagglutinin were added to dilutions of homologous antiserum at *p*H 7·6 (at which the cells would not spontaneously agglutinate) agglutination occurred. This did not occur with normal unsensitized cells. Analogous results were obtained with West Nile, Uganda S, Zika and dengue-2 viruses.

This test of agglutination of sensitized erythrocytes by antibody was applied to serial specimens of serum from rabbits inoculated with Japanese encephalitis virus in parallel with neutralization, haemagglutinin-inhibition and complement-fixation tests. Agglutinating antibody appeared 48 hours after infection and increased to a maximum after 14 days. Cross-reacting antibody in much lower titre was detected with dengue-2 sensitized cells. Analogous results were obtained with rabbits inoculated with dengue-2 virus. Paired acute and convalescent-phase sera from suspected cases of Japanese encephalitis were tested by the same 4 tests and the sensitized cell test gave essentially similar diagnostic information.

C. E. Gordon Smith

GAIDOMOVICH, S. I. & OBUKHOVA, V. R. **Sensitivity of Sheep Embryo Kidney Epithelium Cultures to Japanese B and Tick-Borne Encephalitis Viruses.** *Problems of Virology*. London. 1960, v. 5, No. 3, 331–6, 2 figs. [11 refs.] [Translated from Russian.]

"(1) Japanese B, tick-borne encephalitis and equine encephalomyelitis viruses multiply actively in sheep embryo kidney epithelium cultures.

"(2) Multiplication of Japanese B encephalitis and equine encephalomyelitis viruses is accompanied by a distinct cytopathogenic effect."

FAN, Tsei-Ming, LEVKOVICH, E. N. & FOKINA, K. V. **Cultivation of Japanese B and West Nile Viruses in Cultures of AS, Detroit-6, Hep-2 and Monkey Kidney Cells.** *Problems of Virology*. London. 1960, v. 5, No. 1, 40–45. [Translated from Russian.]

AS (continuous line from an angiosarcoma), Detroit-6, Hep-2, and monkey kidney cell-cultures were infected with 7 strains of Japanese encephalitis (JE) virus and with West Nile virus. When AS cells were infected with mouse-brain suspensions of 4 JE strains only about 30% of the cells were destroyed but after 4 passages the cytopathic effect (CPE) was almost complete. The K-2 strain of JE caused marked CPE from the 1st passage 3–4 days after infection. The K-4 and Nakayama strains affected 25–75% of cells only after 7–12 passages. West Nile caused marked CPE after 2–4 days from the 1st passage. All strains multiplied well in AS cultures. In Detroit-6 cells only 1 of 4 JE strains produced an irregular CPE although multiplication occurred. West Nile caused CPE 5–8 days after infection. In Hep-2 cells 1 of 2 JE strains and West Nile caused marked CPE from the 1st passage and all multiplied. In monkey kidney cells 2 strains of JE and West Nile virus multiplied without causing CPE.

C. E. Gordon Smith

FEDOROV, I. V. **Multiplication of Tick-Borne Encephalitis Virus in Various Parts of the Developing Chick Embryo and the Possibility of their use in Production.** *Problems of Virology*. London. 1960, v. 5, No. 1, 28–31. [Translated from Russian.]

The Sof'in strain of tick-borne encephalitis virus was grown in chick embryos 8–10 days old incubated at 37°C. [route of inoculation not stated]. After 48–72 hours' incubation maximum titre was found in the embryo body (6·5–7·7 log), followed by the yolk sac (5·9–6·3), chorio-allantoic membrane (5·3–5·6), amniotic fluid (4·6–5·3), and allantoic fluid (4·1–5·7). Vaccines were prepared from the bodies, the membranes and the fluids and inactivated with 0·075–0·2% formalin for 4 days at 18°C. and then 15 days at 4°C. Mice were immunized [? dosage] with these and challenged with the Sof'in and Kargasokskii strains. Highest protection indices were obtained with 0·075% formalin: bodies 5372, membranes 4676, fluids 130. Live vaccines of body and membranes were inoculated into rabbits which developed high

neutralizing antibody titres by 36 days after inoculation. Similar vaccines were purified by precipitation with ethyl alcohol: inoculated into rabbits, the vaccine made with bodies gave high antibody responses but that made from membranes gave a poor or negative response.

C. E. Gordon Smith

LEVKOVICH, E. N. & KARPOVICH, L. G. **Comparative Study of the Viruses of the Tick-Borne Encephalitis Group in HeLa Cell Cultures.** *Problems of Virology.* London. 1960, v. 5, No. 1, 31–40, 5 figs.

25 strains of virus from the Russian spring-summer complex (10 tick-borne encephalitis, 6 biphasic meningo-encephalitis and related strains, 2 louping ill, 4 Omsk haemorrhagic fever, 3 Kyasanur Forest disease) were grown in a strain of HeLa cells from the Pasteur Institute, Paris. All strains were successfully carried through 7 or more passages in HeLa cells. After 5 or more passages culture fluids titrated in mice averaged 2·0–2·5 log less than the original mouse-brain material. The maximum titre with louping ill was reached after 4 days, with Kyasanur Forest and Omsk after 5 days, with biphasic meningo-encephalitis after 6 days, and with tick-borne encephalitis after 7 days. Louping ill gave marked cytopathic changes after 3–5 days and after passage the titre in HeLa cells was almost as high as in mice. None of the tick-borne encephalitis strains caused cytopathic changes. After passage biphasic meningo-encephalitis strains produced slight cytopathic changes with high virus concentrations only. Kyasanur Forest strains caused marked cytopathic changes from after 3–4 days' incubation. Omsk haemorrhagic fever strains caused less marked cytopathic changes after 5–6 days but these did not affect all the cells. Titres by infectivity in mice were compared with titres by cytopathic changes in HeLa and cynomologous heart cells: 3 Russian tick-borne encephalitis strains gave titres of 7·2–8·2 log in mice, 5·3–5·8 in heart cells and nil in HeLa cells; 3 Central European strains of tick-borne encephalitis gave similar titres in mice and heart cells and 1·5–3·5 log in HeLa cells; a biphasic meningo-encephalitis strain titred 7·5 in mice, 5·7 in heart cells and 1·7 in HeLa cells; a biphasic milk fever strain titred 7·8 in mice, 6·3 in heart cells, and 2·5–3·2 in HeLa cells; and a louping ill strain titred 8·8 in mice, 6·5 in heart cells and 6·2 in HeLa cells.

C. E. Gordon Smith

FEDEROV, N. V. **An Antigen for the Complement-Fixation Test in Tick-Borne Encephalitis. I. Comparison of Tick-Borne Encephalitis Virus Diagnostic Antigen purified with Different Alcohols.** *Problems of Virology.* London. 1960, v. 5, No. 3, 411–14. [Translated from Russian.]

"(1) Brain antigens prepared by purification of tick-borne encephalitis virus with methyl and ethyl alcohols possess marked complement-fixing properties.

"(2) In production of diagnostic antigen for the complement-fixation test the virus may be purified with ethyl alcohol."

GRESÍKOVÁ, M., HAVRÁNEK, I. & GÖRNER, F. **The Effect of Pasteurisation on the Infectivity of Tick-Borne Encephalitis Virus.** *Acta Virologica.* Prague. 1961, Jan., v. 5, No. 1, 31–6, 2 figs. [13 refs.]

The "holding" method of pasteurization (63°C. for 30 minutes) for milk infected with tick-borne encephalitis virus had previously been shown ineffective [this *Bulletin*, 1960, v. 36, 828]. High temperature short-time methods were therefore investigated. The Hypr strain of virus in its 51st mouse-passage was used. Centrifuged infected mouse-brain was mixed with milk and naturally infected goats' milk was also used. Pasteurization was carried out in an apparatus based on Lindquist's micro-pasteurizer which is described in full. Virus was titrated by intraperitoneal inoculation of mice followed by 2 blind passages where negative and the Storch peroxidase reactions were used as an additional control. 55°C. for 10 seconds reduced the virus titre by only 1·7–>3·0 log and did not affect the positivity of the Storch test. 60°C. for 10 seconds destroyed small amounts of virus but not larger amounts and also did not affect the Storch test. 65°C. for 10 seconds destroyed virus in concentrations up to 5·1 log but not 6·7 log completely and also left the Storch test positive. 72°C. and higher for 10 seconds destroyed concentrations of 6·7 log completely and rendered the Storch test negative. This method with a temperature of 85°C. is now in routine use in Czechoslovakian dairies. The average virus concentration in infected goats' milk was 3·7 log. *C. E. Gordon Smith*

BENDA, R. & DANES, L. **Study of the Possibility of preparing a Vaccine against Tick-Borne Encephalitis, using Tissue Culture Methods. V. Experimental Data for the Evaluation of the Efficiency of Formol Treated Vaccines in Laboratory Animals.** *Acta Virologica.* Prague. 1961, Jan., v. 5, No. 1, 37–49. [18 refs.]

Tick-borne encephalitis vaccines prepared in chick embryo tissue cultures [this *Bulletin*, 1960, v. 35, 717, 941; 1961, v. 36, 380] were tested by a variety of methods. 3 types of mouse resistance test with different dosage schedules were compared and differences as large as 2 log protection were found with the same vaccine. Similar degrees of difference were observed when the sera of these mice were tested for neutralizing antibody. A 3-dose schedule with intervals of 3 and 11 days was found most sensitive. As measured by the neutralizing antibody response of guineapigs, subcutaneous inoculation (3 doses) was more sensitive than intramuscular inoculation. Complement-fixing antibody was not detected in vaccinated guineapigs. With a few exceptions good correlation was obtained between the results of mouse resistance and guineapig neutralizing antibody tests. Chicks showed poor antibody responses to the vaccines. Monkeys in a small experiment showed very good responses to a highly potent vaccine.

C. E. Gordon Smith

BÁRDOS, V. **The Tahyna Virus. I. Study of its Resistance to the Action of some Physical Factors and Chemical Agents.** *Acta Virologica.* Prague. 1961, Jan., v. 5, No. 1, 50–56.

3 strains of Tahyna virus adapted to mouse-brain and one isolated and maintained by intramuscular inoculation of hamsters were used. Heating at 37°C. for 24 hours reduced the titre of a mouse and the hamster-strain by 4–5 log. At 4–6°C. a mouse-strain survived 30 but not 39 days. At −15°C. it decreased in titre by 2·0, 2·9 and 4·1 log after 57, 70 and 94 days respectively. 56°C. for 35 minutes did not completely destroy infectivity. The extraneural strain heated at a range of temperatures for 30 minutes showed no significant loss of titre at 45° and 50°C. but lost 2·0–4·5 log at 55°C. and all infectivity at 58° and 60°C. The surviving mice in this experiment were challenged and inapparent infections demonstrated [or at any rate immunization] with virus heated at 55° but not 60°C. The virus withstood lyophilization well. 2 log of virus was sedimented by 3,700 g×30 minutes or 20,000 g×45 minutes. 2·0 log was also removed by bentonite adsorption, the initial titres in all these experiments being 5·0–6·4 log. Treatment with ether in the cold for 24–48 hours reduced the titre by 1·8–3·1 log. Similar treatment with chloroform reduced the titre by 3·0–3·8 log. Treatment with freon [? at room temperature] reduced the titre by 1·4 log after 1 and >3·4 log after 2 extractions. Sodium deoxycholate reduced infectivity by about 2·5 log. Formalin 1:500 completely destroyed infectivity (initially 6·5 log) in 24 hours at 4°C. *C. E. Gordon Smith*

BÖHM, H. Zur Inaktivierung des Virus fixe " Novi Sad ". [**Inactivation of the Novi Sad Strain of Fixed Rabies Virus**] Reprinted from *Monats. f. Tierheilk.* 1960, v. 12, No. 5, 150–56, 2 figs. [21 refs.]

An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 582.]

SWEET, B. H. & HILLEMAN, M. R. **The Vacuolating Virus, S.V.$_{40}$.** *Proc. Soc. Exper. Biol. & Med.* 1960, Nov., v. 105, No. 2, 420–27, 2 figs. [24 refs.]

Many viruses carried by monkeys have been found as contaminants in monkey kidney cultures [for a brief review see TOBIN, this *Bulletin*, 1960, v. 35, 824]. These viruses usually reveal themselves by destroying the cultures and can be passaged in cells of the same species of monkeys. Now a new simian virus designated by HULL, who has worked extensively with these agents [Hull *et al., ibid.*, 1958, v. 33, 1193], as SV40 has been discovered in cultures of kidney cells of rhesus and cynomolgus monkeys which only produces readily visible cytopathic effects in cultures of kidney cells of *Cercopithecus aethiops* (grivet or vervet East African green monkeys). The virus also grows in patas monkey kidney cells and rhesus testes cells but these cells are less sensitive. Primary rhesus monkey, rabbit kidney, and human amnion cells were insensitive as were HeLa, stable amnion, Chang liver and Girardi human heart cell lines.

The cytopathic effect is characterized by vacuoles in ballooning cells without giant cell formation or nuclear changes. The cells eventually become detached from the glass, often leaving a few islands of normal cells. The viruses studied appeared to be antigenically homogenous and different from many simian viruses. However, some virus antisera did neutralize this virus but since they were prepared from virus stocks grown in rhesus or cynomolgus cells, only negative results are meaningful.

The virus was found in all 3 types of Sabin's attenuated poliovaccine seed virus, in seed stocks of adenovirus 1–7, *Myxovirus parainfluenza* type 1 and 3, and respiratory syncytial virus. All these virus stocks were infected rhesus or cynomolgus monkey kidney cell culture fluids. The virus is relatively heat resistant but is readily inactivated by 1/4,000 formalin at 37°C. though slightly more slowly than polioviruses.

Antibodies to this virus do not seem to appear in people given attenuated poliovaccine orally but do occur in those given the vaccine *via* the respiratory tract (MORRIS and HIATT, *Conference on Production and Testing of Requirements for Live Poliovirus Vaccine*, Nat. Inst. Health, Bethesda, Maryland. August 19, 1960). Antibodies did appear in a high proportion of those given killed vaccines prepared from viruses grown on monkey kidney cells. The importance of these agents is discussed from the point of view of killed and attenuated vaccine production: the role of vacuolating virus in the pathogenicity of new respiratory virus grown in monkey kidney cells and tested in man: the confusing effect of vacuolating virus in diagnostic complement-fixing antigens prepared from virus grown on monkey kidney cells. The authors believe that killed vaccines can be satisfactorily made by using virus grown on monkey kidney cells because SV40 is destroyed by formalin. They are considerably less happy about attenuated vaccines.

The virus appears to be very frequent in rhesus and cynomolgus monkey kidney cultures, thus 7 out of 10 lots of rhesus monkey cells contained the agent and 1 out of 10 cynomolgus lots, although 8 cynomolgus lots contained foamy virus which may have obscured detection of SV40. These lots each comprised kidneys from 2–3 monkeys and were from animals used to prepare killed poliovaccine. *A. J. Beale*

IMMUNITY

KOSUNEN, T. & HALONEN, P. **Response of Young Mice of Immunised Parents to Tetanus Toxoid.** *Ann. Med. Exper. et Biol. Fenniae.* Helsinki. 1960, v. 38, No. 3, 256–61, 1 fig. [14 refs.]

To study the effect of passive maternal immunity on the vaccination response of offspring, the authors injected tetanus toxoid into young mice, aged (1) 2–5 days and (2) 8 weeks, which were born of mice half of which had been actively immunized during pregnancy with tetanus toxoid. The acquisition of immunity was tested for, not by antibody level, but by survival after a challenge with varying dilutions of tetanus toxin 6 weeks after immunization. The response of young mice to tetanus immunization was clearly depressed by passive maternal immunity: immediately after birth they tolerated an amount of toxin which was 10,000 times that tolerated by controls, while after 15 weeks the difference was no longer significant. When immunization was begun 8 weeks later, a response was observed, but it was weaker than that in the young of non-immunized parents. In the latter, when immunization was begun only a few days after birth, the response was only slightly weaker than in the young mice immunized for the first time at the age of 8 weeks. *D. A. Cannon*

WILDE, J. & NAUMANN, G. Die Bedeutung von Geschlecht und Körpergewicht für den Immunisierungseffekt. **[Influence of Sex and Body Weight on the Immunization Effect]** *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1960, Dec., v. 120, No. 5, 326–39. [44 refs.]

The English summary appended to the paper is as follows:—

"The sex dependent immunological reactivity is discussed on the basis of a short review of the pertinent literature. The results obtained by immunizing 275 adult cats with Br. abortus Bang are reported. Within an observation period of 26 days the male animals showed a lower immunization effect than the female ones. Sex dependent differences of the protein fractions of normal sera could not be demonstrated. During the immunization course the alpha-2 globulins showed smaller changes in male than in female cats.

"When the animals were divided into body weight groups regardless of their sex, the immunization effect showed no correlation to the body weight. On the other hand, the serum protein fractions showed body-weight-depending differences, as well in normal, as in postimmunization samples. The possibility of an additional influence of the age of the animals is stressed."

WEIGLE, W. O., COCHRANE, C. G. & DIXON, F. J. **Anaphylactogenic Properties of Soluble Antigen-Antibody Complexes in the Guinea Pig and Rabbit.** *J. Immunology.* 1960, Nov., v. 85, No. 5, 469–77. [28 refs.]

In order to investigate further the anaphylactogenic properties of antigen-antibody complexes and the mechanism responsible for their pathogenic activity, the authors compared the reactions produced by the injection of such complexes into normal animals with the reactions produced by the injection of antigen into either actively or passively sensitized animals. Bovine serum albumin, bovine gamma globulin and egg albumin were used as antigens and antisera to these were prepared in rabbits. Anaphylactic reactions were produced in guineapigs and rabbits by the intravenous injection of soluble antigen-antibody complexes. In the guineapig the symptoms, the emphysema produced in the lungs and the inhibition of symptoms by antihistamine were similar to those observed in the classical passive and active anaphylactic reactions. By trace-labelling the antigens with ^{131}I, the authors found that there was a preferential localization of the ^{131}I activity in the lungs of guineapigs during the resulting anaphylaxis, and this localization was more marked in animals dying in anaphylaxis than in those having only mild reactions. A prior injection of antigen into guineapigs increased the severity of the reactions produced by a subsequent injection of soluble antigen-antibody complexes. Considerable complement activity was removed from the blood of guineapigs injected with the soluble antigen-antibody complexes, even when no, or only mild, anaphylactic symptoms occurred; it was thought that the rate at which complement was fixed might be more important than the total amount fixed. Complement seemed to have a role in anaphylaxis but the nature of this role was not completely clear. *D. A. Cannon*

KAHN, R. L., KIM, S. H., CURTIS, A. C. & SIMONS, C. S. **X Irradiation and Toxin Neutralization by Antitoxin.** *J. Infect. Dis.* 1960, Nov.–Dec., v. 107, No. 3, 325–31, 1 fig. [10 refs.]

This paper deals with one aspect of the neutralization of diphtheria toxin in normal rabbits by the injection of homologous horse serum diphtheria antitoxin, *viz.* the localization of the toxin-neutralizing fraction of the antitoxin and the consequent delay in its reaching, and acting upon, the toxin. The question arose as to how much antitoxin would be necessary for the neutralization of a dose of toxin injected into an X-irradiated area of tissue of normal rabbits compared to the same dose injected into a corresponding area in non-irradiated animals. The results indicate that a restricted amount of antitoxin injected subcutaneously in an irradiated area up to 7 days after exposure to 1000 r was more effective in the neutralization of a lethal dose of toxin than the same amount injected into a corresponding area of non-irradiated rabbits, and the most marked neutralization occurred 24 hours after exposure: by 14 days after exposure the neutralization of the toxin was comparable with that in control animals, but 90 days after, no neutralization of the toxin was observed. These rather unexpected results, the authors think, indicate that fundamental data are required on the effect of focal irradiation on the phenomena of the neutralization of toxin by tissue-injected antitoxin and the localization of tissue-injected proteins. *D. A. Cannon*

LIU, C. **Studies on Primary Atypical Pneumonia. III. A Factor in Normal Serum which enhances the Reaction between PAP Virus and Convalescent Serum.** *J. Exper. Med.* 1961, Jan. 1, v. 113, No. 1, 111–23. [16 refs.]

In continuation of his work on the virus of primary atypical pneumonia (PAP) [this *Bulletin*, 1958, v. 33, 190; 1959, v. 34, 988] the author here describes a factor encountered in fresh normal human (or guineapig) serum which enhances the PAP antibody titres in serological reactions with its homologous virus as tested by indirect fluorescent antibody staining. He thinks that this factor is not properdin: serum lacking properdin showed full enhancing activity. Its identity is not established, but it appears to be a part of complement: C'1, C'2, and C'4 are essential components, but C'3 is not. It is possible that the factor may act as a catalyst to increase the deposition of antibody molecules on the viral antigen, or it may help to form a firmer union between the antigen-antibody complex preventing the washing away of antibody molecules during the various steps of fluorescent staining procedures. At any rate the addition of this enhancement factor to human sera convalescent from PAP has made the serological test more sensitive without affecting its specificity. *D. A. Cannon*

KLEIN, P. & COLLI, A. Herstellung und Auswertung von "Anti-Komplement". **[Preparation and Use of Anti-Complement Immunity]** *Ztschr. f. Hyg. u. Infektionskr.* 1961, v. 147, No. 3, 201–12, 2 figs. [13 refs.]

CIBA FOUNDATION [WOLSTENHOLME, G. E. W. & O'CONNOR, M., Editors]. **Cellular Aspects of Immunity.**

This book was reviewed on p. 418.

Miscellaneous

WILLIE, C. V., HARRIS, Virginia G. & WEHRLE, P. F. **The Epidemiology of Accidental Poisoning in an Urban Population: I. Selection of the Population Sample and Interviewing Technics.** *Amer. J. Pub. Health.* 1960, Nov., v. 50, No. 11, 1705–9.

WEHRLE, P. F., DAY, P. A., WHALEN, J. P., FITZGERALD, J. W. & HARRIS, Virginia G. **The Epidemiology of Accidental Poisoning in an Urban Population. II. Prevalence and Distribution of Poisoning.** *Amer. J. Pub. Health.* 1960, Dec., v. 50, No. 12, 1925–33. [15 refs.]

In the first part of this study [above] the selection of the study population and the method of interviewing each of the random sample of 1,069 families in Syracuse, N.Y. were discussed. The results of the study are here described with 8 tables.

The types of products causing poisoning were similar to those recorded in other surveys in that the medicine group of which aspirin was the most important were more frequently ingested than the miscellaneous group which included household and petroleum products, pesticides, paint and cosmetics. The family interviews showed that there had been considerably more cases of poisoning than had been reported to physicians, hospital or poison centre. It was noted that the proportion of persons who required advice or treatment was not different in the various socioeconomic groups studied. Information is also given on poisoning episodes by age and sex, multiple episodes of poisoning in families and the place in the home where the materials which caused poisoning had been kept.

Most of the episodes of poisoning were in young children and 12% of children aged 2 years had experienced poisoning within the 12 months prior to the study. Lack of awareness of the potential hazard of household medicines and other products was common and the need for continued education of parents is emphasized. *M. E. Delafield*

CANN, H. M., ISKRANT, A. P. & NEYMAN, Dorothy S. **Epidemiologic Aspects of Poisoning Accidents.** *Amer. J. Pub. Health.* 1960, Dec., v. 50, No. 12, 1914–24, 5 figs. [13 refs.]

In 1957 the U.S. Public Health Service organized the "National Clearinghouse for Poison Control Centers". 59 of these centres located in 20 states have submitted 15,094 individual case reports in the period January 1, 1954 to December 31, 1958. Of these cases 14,069 have been classified as poisoning accidents due to the ingestion of poisons or potential poisons and supply the data for the detailed analysis contained in this paper.

About 90% of the poisoning accidents involved children under 5 years of age and most of the study concerned this age-group. Details of the analysis are described with figures and tables. The particulars given are the age distribution of these accidents, specific type of poisonous product by age of patient, type of product as a percentage of all ingestions at different ages, types of container used for the poisonous product, the regional frequency of the poisoning by different substances, seasonal frequency and the room of the house where the poisonous substance was found.

There is a long discussion of the results which are largely in accord with other published reports [this *Bulletin*, 1957, v. 32, 108, 718; 1958, v. 33, 924; 1959, v. 34, 1069; 1961, v. 36, 219 and above] but many more studies are needed in order to understand more fully the "causative mechanisms underlying" these poisonings. *M. E. Delafield*

McDONALD, R. **Accidental Poisoning in Children in Cape Town, with special reference to Kerosene and Salicylates.** *South African Med. J.* 1961, Jan. 14, v. 35, No. 2, 21–5. [19 refs.]

In the period 1951–58 the total number of children admitted to 2 hospitals in Cape Town for accidental poisoning was 166. The highest incidence was in those aged 1–2 years (49%) and the lowest in those aged 0–1 years (5%). These figures when compared with those reported from Johannesburg and 2 Scottish hospitals are but little different. The commonest poisons ingested in the Cape Town experience were kerosene (43 cases), barbiturates (21), arsenic (19), salicylates (14), caustic soda (3) and ferrous sulphate (4).

Arsenic poisoning seems to be relatively more common in Cape Town than elsewhere and is due mainly to the ingestion of ant-poison. There was 1 death among the 19 cases. All the children who had taken barbiturates recovered completely.

Most of the paper is devoted to kerosene and to salicylate poisonings and their treatment. In the kerosene poisonings clinical recovery was rapid in most cases although X-ray evidence of pulmonary involvement mainly of the basal zones was found in nearly every case. There is a discussion of some of the conflicting opinions in published work on the question of how the kerosene reaches the lungs with the conclusion that the "respiratory pathology is probably solely the result of aspiration, and gastric lavage is to be deprecated".

Salicylate poisoning is considered at some length because of its frequency and importance. There is a full account of its symptomatology, mortality, pathology and the biochemical disturbances it induces. The treatment of the poisoning is discussed under the headings of the role of lavage and on the controversial question of whether to give alkalis or not. A suggested plan of treatment is offered in which there is mention of published reports on the value in severe cases of exchange transfusion and extracorporeal dialysis.

M. E. Delafield

SHARMA, R., GAMBHIR, M. S. & JAIN, V. C. **Accidental Poisoning in Childhood.** *Indian J. Child Health.* 1961, Jan., v. 10, No. 1, 21–33, 2 figs. [26 refs.]

Only a few studies of accidental poisoning in children have as yet been made in India but these—from Bombay, Amritsar, Nagpur and Indore—have shown that the pattern of poisoning in India is different from that reported from the United States and Great Britain [this *Bulletin,* 1959, v. 34, 848].

This paper contains a report on 146 cases of accidental poisoning in children under 16 years of age admitted to the SMS Hospital, Jaipur, during 1951–59. These cases in childhood represent 43·7% of the total of 334 accidental and intentional poisonings admitted during the same period.

The data of the 146 cases in childhood were analysed by age-groups (0–1, 1–4 and 5–15 years), nature of poison (household substances, medicaments, plants and seeds and miscellaneous), sex, religion, time of day and month and by place of accident.

Children 1–5 years of age showed the highest incidence (52%) of all the poisonings but the frequency of poisoning due to medicaments was greatest in the infant 0–1-year group. In general males (62%) suffered more poisonings than females (38%).

Among household substances kerosene (26 cases) and copper sulphate (17 cases) were found to be of most importance. The copper sulphate poisonings were restricted largely to Hindus because this substance is so much used by them "as a part of white-washing material" particularly at the time of Hindu festivals. Opium which with 33 cases of poisoning was the most frequent cause in the medicament group had usually been given by the mother to quieten the child or for diarrhoea but in 3 cases had been given by "practitioners of indigenous medicine." Poisoning by plants and seeds (31 cases) was commonest in the older children and datura seeds (24 cases) were the most frequent cause.

There is a discussion of the host, environmental and social factors involved in this accident problem with a statement of the preventive measures which are needed.

M. E. Delafield

KOSSICK, P. **Accidental Paraffin Poisoning.** *South African Med. J.* 1961, Feb. 11, v. 35, No. 6, 112–13.

This is a short paper on accidental poisoning by paraffin in children in South Africa where this poisoning is the commonest type. Paraffin is widely used among the non-White population.

61 patients were treated during January–December 1959 at the Livingstone Hospital, Port Elizabeth, for paraffin poisoning. Their ages ranged from 9 months to 19 years and 21 were female and 40 male. The symptoms are described shortly. Some of the patients were examined by X-ray which showed non-specific atelectatic and consolidating lesions mostly in the lower lobes in 60% of cases.

10 patients were admitted to hospital and the remainder "were given antibiotics and chemotherapy, discharged, and told to return for follow-up at the outpatient department". Gastric lavage was not carried out. At follow-up examination a year later only 30 of the patients were available and of these 28 were fit and well but 2 had developed pulmonary tuberculosis.

M. E. Delafield

McLAUCHLAN, G. P., IRVINE, E. D., KEEN, J. H. & BRIMBLECOMBE, F. S. W. **Home Accidents in Exeter Children.** *Med. Officer.* 1961, Mar. 3, v. 105, No. 9, 115–19.

This paper is in 2 parts:—(1) a survey of home accidents in children in Exeter in 1958 and (2) a review of all children admitted to the Royal Devon and Exeter Hospital during 1953–59 as a result of burns or scalds.

The survey was small and concerned 91 accidents, particulars of the children having been obtained from the casualty officer at the hospital and from 3 general practitioners. Health visitors made their enquiries at the homes of all the children. The accidents were classified

into 4 groups: falls (43 accidents), burns and scalds (26), poisoning (5) and wounds, etc. (17). Analysis of the data showed that 68% of the accidents were in boys, 70% involved children over 1 and under 5 years old and that 80% occurred in the colder months of the year. It was also found that the number of accidents in only children was small but was relatively high in families with 3 or more children. Study of the social class distribution of accidents showed little significant difference between the actual and expected number of accidents. There is a description and discussion of the different types of accident and the way in which they were caused.

In the second part of the paper there is an analysis of 113 cases of burns or scalds in children living in or outside Exeter treated at the hospital in 1953–59. There were 77 scalds and 36 burns. The circumstances of these accidents are described. Scalds were generally less severe than the burns but occurred with greatest frequency in small children involving them sometimes in long periods of hospitalization and often some permanent scarring.

[See also this *Bulletin*, 1954, v. 29, 217; 1959, v. 34, 963.] *M. E. Delafield*

CASS, J. S., CAMPBELL, Irene R. & LANGE, Lilli. **A Guide to Production, Care and Use of Laboratory Animals. An Annotated Bibliography.** *Federation Proc.* Wash. 1960, Dec., v. 19, No. 4, Pt. 3, Suppl. 6, pp. vi + 196.

Book Reviews

BROCK, J. F. [D.M., F.R.C.P.]. **Recent Advances in Human Nutrition with special reference to Clinical Medicine.** With a number of invited contributions on special subjects. pp. xii + 454, illustrated. 1961. London: J. & A. Churchill Ltd., 104, Gloucester Place, W.1. [50s.]

The first 175 pages of this large book have been written by Professor Brock, who is Professor of Medicine in the University of Cape Town. The remainder consists of the following contributions on special subjects: *Dietary Fats* by B. BRONTE-STEWART; *Abnormalities of Fluid and Electrolyte Metabolism in Malnutrition*, (a) *In Adults* by L. EALES, (b) *In Infants* by J. D. L. HANSEN; *Nutrition Research in Spanish-Portuguese Speaking Countries* by M. A. GUZMÁN, W. ASCOLI and N. S. SCRIMSHAW; *Bacterial Symbiosis in the Gastro-Intestinal Tract* by P. GYÖRGY; *Protein Malnutrition and its Prevention and Treatment with Special Reference to Kwashiorkor and Marasmus* by J. D. L. HANSEN; *Trends in Infant Nutrition* by L. E. HOLT; *Effects of Altered Nutrition on the Skeletal System* by W. P. U. JACKSON; *Nutrition in Old Age* by K. JAHNKE; *The Effects of Altered Nutrition on the Function of the Endocrine Glands* by A. O. LURIE and W. P. U. JACKSON; *Protein Values of Human Foods* by B. S. PLATT, D. S. MILLER and P. R. PAYNE; *Nutrition and Infection* by N. S. SCRIMSHAW; *Cardiopathy of Unknown Origin in Africa* by J. G. THOMSON; *Trends in Nutrition in the French-speaking Countries* by J. TREMOLIÈRES; *Nutritional Anaemia with Special Reference to Tropical Regions* by A. W. WOODRUFF; *Human Nutrition and the United Nations Agencies* by WHO and FAO.

Of the special contributors, five are associated with the University of Cape Town. Brock justifiably comments that "Cape Town has proved to be a fertile field for the study of clinical nutrition".

The part of the book written by Brock himself is called *General Review of Trends*, and with respect to trends he makes a number of important points. In the first paragraph of the Introduction, he refers to the rediscovery by medicine and public health "of amino acids and fatty acids, interest in which had, up to 1950, largely been submerged by an almost exclusive preoccupation with vitamins on the part of clinicians and public health workers". This change in outlook is evident in the book as a whole, a large proportion of which is devoted to dietary proteins and protein malnutrition, and to dietary fats with special reference to the possible relationship between the amount and nature of fat intake and degenerative heart disease. The vitamins and minerals are indeed adequately covered, but do not occupy a central position in the picture. Another new development to which due weight is given in the book is the increasing contribution which has been made by the United Nations Agencies, WHO and FAO, in the study of, and attack on, problems of nutrition throughout the world. This emphasis may be partly due to the fact that the author and many of the special contributors have been personally associated with the United Nations nutrition programme, but it also reflects the rapid development of that programme and the coordinating role which these Agencies have played, particularly in the field of protein malnutrition.

Among the chapters of special interest to clinicians in the *General Review of Trends* are those on *Dietary Fats, Dietary Proteins, Infant Feeding, The Effect of Malnutrition on Individual Systems* and *Acute Deficiency and its Correction*. In considering the future the author has some wise comments to make on population and food supply, nutrition education in the medical school and hospital, food faddism and various other important issues. The 462 references which conclude the review are evidence of his wide reading and broad knowledge of the subject.

The second part of the books opens with an article by Bronte-Stewart on *Dietary Fats*, summarizing clearly the findings underlying the hypothesis that a disordered

lipid metabolism over the years " leads to atherosclerosis and possibly is one of the major contributing factors to the final picture, ischaemic heart disease ". " These implications ", the author adds, " are wide, affecting developments in animal husbandry, food processing and the education of our youth ". The prevention and treatment of protein malnutrition is discussed by Hansen, largely on the basis of direct experience in South Africa; this article links up closely with the article on *Protein Values of Human Food* by Platt, Miller and Payne, which describes recent work in the Human Nutrition Research Unit in Mill Hill on methods of predicting the protein values of individual foods, meals and diets. The difficult subject of *Nutrition and Infection* is lucidly discussed by Scrimshaw, again on the basis of direct experience, in this instance in Central America. *Nutritional Anaemia with Special Reference to Tropical Regions* is reviewed by Woodruff, who describes the various types of anaemia found in the tropics and their probable aetiology, rightly pointing out that " the incidence of nutritional anaemia in the tropics is much greater than elsewhere and a common observation by practitioners there is that very many of their patients are, to a greater or lesser extent, anaemic ".

Trends in nutrition in French-speaking countries are dealt with in a chapter by Tremolières, who comments that, while there is a growing interest in nutrition in these countries, few clinical groups have a structure which allows for research. Three workers from the Institute of Nutrition for Central America and Panama —Guzmán, Ascoli and Scrimshaw—present a chapter, with 241 references, on nutrition research in Spanish-Portuguese speaking countries, which shows the impressive amount of research, mainly on protein malnutrition, which has been done in Latin America during the past decade. Recent German literature on nutrition in old age is reviewed by Jahnke in an article which, through no fault of the author, is uninforming and platitudinous, because little or nothing is at present known about the influence of ageing on nutritional requirements.

This book may be strongly recommended to doctors interested in nutrition both in the developed and underdeveloped countries, as well as to nutrition specialists. It covers ground at present largely unfamiliar to the medical profession, providing a survey of trends and advances in nutrition research and applied nutrition not available in any other publication. *W. R. Aykroyd*

ARMITAGE, P. [M.A., Ph.D.]. **Sequential Medical Trials.** 105 pp. illustrated. 1960. Oxford: Blackwell Scientific Publications. [20s.]

The efficacy of a new prophylactic or therapeutic preparation or procedure can seldom be assessed without recourse to a controlled medical trial. During the last 25 years many " treatments " have been submitted to trials conducted under a variety of conditions. Most modern trials have in common the random allocation of experimental units to different treatment groups; the assessment of response to treatment by investigators unaware of the treatment being received by any given experimental unit and the ultimate comparison of " average " responses between treatment groups. An experimental unit is usually a human subject, but in some cases two or more periods of treatment on one subject can yield correspondingly two or more experimental units—trials between subjects are therefore distinguished from trials within subjects. In non-sequential designs the number of experimental units required in a trial is predetermined and no comparison between treatment groups is attempted until the assessments of response have been made on all units. In such experiments an estimate of the number of units required is based on decisions being taken in advance on (1) the minimum difference between treatment groups which for clinical or biological reasons it is important to detect, (2) the probability of rejecting the null hypothesis that no such difference exists when that hypothesis is true (2α in the notation used), and (3) the probability of accepting the null hypothesis when, in fact, it is false (shown as β). Thus $(1-\beta)$ is the power of the trial to detect the critical value associated with the first decision at a significance level of $P=2\alpha$.

Recently trials have been conducted by sequential methods which demand the same advance decisions, preserve most of the factors of random allocation of experimental units to treatment groups and the so-called " blind assessment " of response to treatment, but which permit continuous analysis of the assessments as they accumulate during the progress of the trial. In such a trial the number of experimental units required is not predetermined and the trial stops as soon as a suitable decision is reached. Such methods are based mainly on WALD'S statistical theory of sequential analysis and owe much of their growing popularity to the clear expositions of BROSS in the U.S.A. [this *Bulletin*, 1953, v. 28, 312], and Armitage in the U.K. [*ibid.*, 1954, v. 29, 1269]. Most of the published work has appeared in several statistical and medical journals so that the need for a comprehensive explanation of the technique in a single volume is obvious. Armitage's simply written book will admirably satisfy medical needs and probably others as well because the methods have applications outside the sphere of medicine. His aim has been " to write an account of the principles underlying the subject, and to provide sufficient detail about the methods to enable the medical practitioner to proceed without necessarily feeling obliged to consult a statistician ".

The first chapter sets out the main statistical ideas involved in clinical trials in general, emphasizes the concept of evaluating results in terms of preferences and explains the meaning of errors of the first and second kind (α and β respectively) which require consideration in making the second and third decisions mentioned above. In the second chapter the author enlarges upon economy, estimation with desired accuracy and ethical considerations as the main reasons for sequential analysis. Here he makes the distinction between open and closed designs and a category of the latter, which he has developed and has called restricted designs. Most of the book is devoted to closed, including restricted, designs which are probably more suitable for medical experiments. Some hints about situations in which sequential designs are inappropriate are given.

In the third chapter specific plans are tabulated for sequential trials where two treatments are compared and assessed on pairs of experimental units in terms of

preferences. If the treatments given to a pair of experimental units are denoted by A and B, the response of any pair falls into one of three categories of which only the first two are preferences: (1) A better than B, (2) B better than A, and (3) no decision about which is better. Results of the first and second categories are plotted on a diagram in equal spaced movements north-east and south-east respectively until a boundary is reached. Boundaries are drawn in advance and are determined from the decisions about the critical value, α and β. The trial stops when a boundary is reached—the result (at $P=2\alpha$ level of significance) being dependent upon which of the boundaries is reached. In this chapter tables give the necessary numerical information for drawing boundaries for a series of possible preferences; ranging in 5% steps from 55% to 95% of all expressed preferences being in favour of a given treatment, for open and restricted designs when $2\alpha=0{\cdot}05$ with $(1-\beta)=0{\cdot}95$ and when $2\alpha=0{\cdot}01$ with $(1-\beta)=0{\cdot}95$. These tables also show the maximum number of preferences likely to be needed to arrive at a result both by sequential and non-sequential methods. Reference is also made to Bross's closed designs, and plans are given. The chapter includes an example of an open design, a closed design from Bross's plans and two restricted designs; it concludes with plans and an example for so-called skew restricted designs for detecting the superiority of one specific treatment over another as distinct from the preferred treatment of either. [Table 3·10, giving plans for skew restricted designs for $2\alpha=0{\cdot}01$ with $(1-\beta)=0{\cdot}95$ is wrongly headed as it shows $2\alpha=0{\cdot}05$ and no value for $(1-\beta)$. Another misprint occurs on page 40: the power of the test in the 4th line should be $(1-\beta)=0{\cdot}95$.]

The fourth chapter relates evaluation by preferences to the more classical approach used in non-sequential trials of a comparison between two proportions and indicates the application of sequential methods to situations in which assessment on each unit is made in terms of success or failure. Two examples, between and within subjects, set out the procedure. The fifth and sixth chapters deal with quantitative responses to treatment. In the fifth chapter the situation is considered where the variance of the response measurement is known and the critical value (μ) can be expressed as a ratio of the standard deviation (μ/σ); for values of (μ/σ) from 0·2 to 1·4 plans are tabulated for $2\alpha=0{\cdot}05$ with $(1-\beta)=0{\cdot}95$ for open and restricted designs when dealing with normally distributed measurements. If δ is the difference between measurements of a pair of experimental units a quantity $\Sigma\delta$ is continuously estimated and plotted on the sequential diagram. In the sixth chapter the more usual situation where little is known about σ is considered; here a quantity $z=(\Sigma\delta)^2/\Sigma\delta^2$ is estimated continuously and plotted as the results accrue and a sequential "t" test results. Again designs for open, closed and skew trials are discussed and an example of each is included. The seventh chapter is briefly concerned with follow-up studies, the eighth deals with comparisons of treatments against known standards and the estimation of relative efficacy of treatments, while the ninth deals with "misconceptions and difficulties".

Mathematical proofs do not appear in the chapters although throughout references to the original theory are given. For interested readers some statistical notes appear in the appendix to cover theory not easily obtained elsewhere. Armitage describes the procedures with admirable clarity, but as his preface encourages medical practitioners to proceed unaided by statisticians, it is to be hoped that by the time the next edition is prepared the further use of these methods, which this book is bound to encourage, will enable him to include rather more practical examples with their completed diagrams. The careful non-statistical research worker, however, will have no difficulty in designing a trial, suitable for most situations which he is likely to encounter, with the aid of the excellent tables of plans which are easily understood and used once the definitions of less than a dozen symbols are learnt. A good bibliography completes this excellent little book, which by modern standards is a real bargain at its present price.

E. A. Cheeseman

POOL, W. A. [M.R.C.V.S.] [Editor]. **The Veterinary Annual.** 2nd issue. pp. xxiv + 359, numerous illustrations. 1960. Toronto: The MacMillan Co. of Canada Ltd. Baltimore: The Williams & Wilkins Co. Bristol 4: John Wright & Sons Ltd., The Stonebridge Press, Bath Road. [38s. 6d.]

Attempts have been made to gather into one small volume 8 special articles of veterinary interest, and summaries of the recent veterinary literature published throughout the world. The special articles range from accounts of veterinary medicine and affairs in Great Britain, the U.S.A. and France, to the challenge of *Brucella* and the relationship of "the child, the pony and the veterinary surgeon". The greater part of the book is concerned with reviews of those papers of interest published within the last year or year and a half. The arrangement is by subjects and there are thus chapters on diseases relating to bacteria and fungi, to protozoa and the viruses. Parasitology stands alone, unencumbered by diseases to which the subject may be related. Other chapters are concerned with veterinary physiology, public health, neoplasms and diseases associated with poisons, radiation, faulty nutrition and metabolic upsets. A short account is given of new drugs and appliances, and there is a note on legal matters. An index is provided and this is preceded by an incomplete list of English veterinary works and new editions published during the last 12 months.

The pattern is similar to the first edition [this *Bulletin*, 1960, v. 35, 1069], and the second issue is a demonstration of the courage of the editor. Over 30 contributors, most of whom helped in last year's issue, have attempted this difficult task. They have compiled an immense amount of information, but it is neither critical nor digestible; nevertheless it is a valuable compilation. Laboratory workers and field workers, whether at home or overseas, will find at hand recent information available on almost any veterinary topic. Summaries, though uncritical, will be found and these will enable one to delve more deeply into the subject selected. From this it will be possible to trace literature which is relevant. For the uninitiated the book will be of less value.

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